A Comparative of Ginger Extract in Nanostructure Lipid Carrier (NLC) and 1% Diclofenac Gel for Treatment of Knee Osteoarthritis (OA)

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Objective: *To compare and evaluate the efficacy of ginger (Zingiber officinale Roscoe) extracts in NLC for treatment of osteoarthritis of knee compared to 1% diclofenac gel as an active control.*
Material and Method: *One hundred twenty patients age 50 to 75 years with OA knee, based on the American College of Rheumatology (ACR) criteria were randomized into two groups receiving ginger extracts in NLC and control 1% diclofenac gel for 12 weeks. The efficacy of treatment was monitored at 4, 8, and 12 weeks by using the WOMAC composite index and the Patient Global Assessment (PGA). The t-test was used to compare the mean scores at baseline in each group. Repeated ANOVA was used to compare the mean scores, and Chi-square test was used to compare the dichotomous variables between the two groups at 4, 8, and 12 weeks.*
Results: *One hundred eighteen participants completed the study and were included in the ITT efficacy analysis. Both ginger extract in NLC and diclofenac gel could significantly improve knee pain, stiffness, physical function, and PGA following 12 weeks of treatment. In the repeated ANOVA, there were no differences in the result between these two groups. The response rate for at least a 50% reduction in pain was significantly greater following Ginger extract in NLC treatment compared to topical diclofenac [40/59 (67.7%) vs. 27/59 (45.7%) $p<0.05$]. There were no significant adverse events.*
Conclusion: *Ginger extract in NLC relieves pain, improves function, and improves the Patient Global Assessment in OA knee during a 12-week treatment.*

Keywords: *Osteoarthritis, Ginger, Zingiber officinale Roscoe, NLC*

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Osteoarthritis (OA) is one of the most common joint disorders, and the evidence shows that it affects more than one-third of people older than 65 years. Patients with OA are at a higher risk of death compared to the general population as shown by odds ratio of 1.54[1]. The pathophysiology of OA is associated with degeneration of articular cartilage. It is mediated by distinct factors like inflammatory mediators, biochemical factors, changes due to ageing, and metabolic factors. It causes dominant disability to patients, characterized by rolling incidents of pain, stiffness, loss of function, and disability to perform activities. Clinical findings comprise of crepitus, tenderness, and joint swelling[2,3]. The end point of treatment is to relieve pain and improve mobility of joints. The pharmacological treatment with non-steroidal anti-inflammatory agents includes Acetaminophen, Aspirin, Diclofenac, and selective COX-2 inhibitors like. Celecoxib provides only symptomatic relief. However, the usable drugs have several limitations like gastrointestinal side effects and adverse cardiac events with the use of selective COX-2 inhibitors[4,5]. Due to these limitations, herbal medicines are sometimes needed to provide alternative therapies. Ginger (*Zingiber officinale*) is one of the most commonly used natural products and a promising agent for treatment of OA[6-8]. In animal and human studies, ginger extract has shown to have a significant

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effect in reliving inflammatory symptoms in patients with OA[9,10]. The anti-inflammatory property of ginger is due to its inhibition of COX1, COX2, and LOX[11,12]. Furthermore, it also inhibits several gene encoding cytokines, chemokines, and inducing enzyme COX-2, hence, modulating the biochemical pathways activated in chronic inflammatory process. Unfortunately, the major adverse event with oral ginger is heartburn and gastrointestinal disturbances as to the side effects of oral NSIADs. In addition, active compound such as gingerol and shogal are poorly absorbed and rapidly metabolized in the gastrointestinal system[13-15]. To solve this problem, the topical ginger extract in Nanostructure Lipid Carrier (NLC) forms is preferable to the oral forms.

The ginger extract in NLC preparation is produced by National Nanotechnology Center, National Science and Technology Development Agency, Thailand. The ginger extract in NLC is based on an extract of the rhizome *Zingiber officinale,* in which 5% ginger extract (contains equivalent to 11.8% of active [6]-gingerol), conducted to form a Nanostructure Lipid Carrier, which is prepared by weighing the composition of solid lipid, liquid lipid, surfactant, and water mix. The quality and stability is controlled by physical and chemical stability. This technique of using nanoparticle-based delivery systems has many benefits that include increased biodegradability, biocompatibility, non-toxic, and less expensive[16]. However, there are few studies to show the therapeutic efficacy of topical nanoparticle-based ginger extract in patients with knee osteoarthritis. Therefore, we conducted a clinical study to assess the efficacy and safety of ginger extract in Nanostructure Lipid Carrier (NLC), which has active amount of [6]-gingerol for topical relief of pain compared with 1% Diclofenac gel in patients with knee OA.

Material and Method

Study design

A 12-week, double-blind, active-controlled, parallel group trial was performed at Tha Chang Hospital, Singburi province between June and October 2014. The protocol followed the 1975 Declaration of Helsinki as revised in 1983 and informed consent was signed by all patients prior to the start of any study-related procedure. It was approved by the Ethical Committee of the Department for Development of Thai Traditional and Alternative Medicine, Ministry of Public Health (Thai Clinical Trial Registry No. TCTR 20140306001). Patients were randomized to receive treatment by a simple random sampling, and both the investigators and the patients were blinded to treatment assignment.

Patients

Patients with OA knee diagnosed by the American College of Rheumatoid Classification Criteria using the decision three format radiographic criteria[17,18]. The radiographic changes include at least osteophytes and correspond to grade 2 and 3 OA according to the Kellgren and Lawrence criteria[19].

Inclusion criteria were (a) age between 50 and 75 years, (b) knee pain of a degree that could be tolerated and alleviated by using acetaminophen as an escape medication for 12 weeks (during the study period). Exclusion criteria were (a) secondary causes of knee OA, (b) history of allergy to medicinal herbs used during study, (c) severe joint instability or severe deformity (OA grade IV Kellgren and Lawrence), or (d) body mass index (BMI) >30 kg/m^2.

After screening, patients entered a 1-week washout period for anti-inflammatory and analgesic medications, during which they were allowed to take acetaminophen 500 mg three times a day (or every 4 to 6 hours) for pain, but no other topical analgesics, or oral NSAID and COX-2 inhibitors. If patients were determined to be eligible for the study, they were randomly assigned to the Ginger extract in NLC group or 1% diclofenac group. The Ginger extract in NLC was applied at a dose of 1 gm three times a day for four weeks and the diclofenac group also received an identical tube containing 1% Diclofenac gel applied similarly.

Treatment

The ginger extract in NLC contained extract of ginger by ratio of 5% by weight ([6]-gingerol content 11.18%). The potency of extract preparation was followed and analyzed for the active molecule 6-gingerol with HPCL. In addition, in vitro studies of release of the preparation was done using modified Franz diffusion cell method and approximately 92% of 6-gingerol from NLC was released within 24 hours.

Assessment

Efficacy of the treatment was assessed using the Western Ontario and McMaster Universities (WOMAC) index that assessed pain, stiffness, and physical function (classified into pain score, stiffness score, and physical function score)[20]. Scores were interpreted in a scale of 0 to 10, with zero representing no knee problems and 10 representing extreme knee problems. Apart from this the Patient's Global Assessment (PGA) was evaluated on a 5-point Likert scale (5 = very poor, 4 = poor, 3 = average, 2 = good, 1

= very good)[21,22]. The responder criteria were defined as per the Outcome Measures in Rheumatology (OMERACT) Committee and the Osteoarthritis Research Society International (OARSI) Committee[23]. It covered three domains (pain, function and PGA), and was defined as a participant with ≥50% improvement in pain or function that was ≥20% of the scale, or ≥20% improvement in at least two domains-pain, function or PGA that was = 10% of the scale from the baseline. Efficacy assessments were performed at baseline and after 4, 8, and 12 weeks of treatment.

Safety was evaluated via laboratory tests and all adverse events including the onset, duration, and intensity (mild, moderate, or severe) of events, as well as the action taken and outcomes were reported. The relationship between an adverse event and study medication was assessed by the investigator as unlikely, possible, probable, and certain. Adverse events were recorded according to Naranjo's Algorithm and World Health Organization (WHO) adverse events terminology[24,25]. Laboratory studies were recorded at baseline and after 12-week of treatment, which included hematology (CBC), blood chemistry, renal function tests (BUN and creatinine), and liver function tests (SGOT, SGPT and ALP).

Sample size

Sample size calculation was based on the ability to detect clinically important difference in mean of pain scores between control group and treatment group. The present study used technical sample size calculation by Cohen J[26]. We used 95% confidential interval, power at 80%, and effect size of 0.15[15] and so a total sample size of 120 participants (60 per treatment group) was specified after adjusting for a 20% drop out, which seemed to be an appropriate sample size.

Statistical analysis

Safety analyses was performed on all randomized patients who received at least one dose of study treatment. There was no imputation of missing safety data. Efficacy analyses was performed with an intention-to-treat (ITT) analysis and any missing efficacy data in the ITT analysis used the Last Observation Carry Forward (LOCF) method LOCF. Baseline demographic and clinical variables were analyzed by Chi-square and Student's t-test. Adverse events incidence was analyzed by Chi-square and Fisher's exact test. Continuous variables (WOMAC dimensions, PGA) were analyzed by repeated ANOVA. The dichotomous variables were analyzed by Chi-square test. All statistical tests were two-sided and were performed at $p<0.05$ level of significance.

Results

Clinical flow chart

One hundred twenty participants were randomized to treatment with either Ginger extract in NLC group (n = 60) or topical diclofenac group (n = 60). All participants received their allocated intervention and 59 (98%) patients in each group completed the entire 12-week treatment. Dropout rate was similar in both groups (Fig. 1).

Safety and efficacy variables showed no statistically significant difference between the treatment groups with regard to important background disease characteristics. All patients with at least one visit after the baseline evaluation were included in the intent-to-treat (ITT) analysis. Two patients, one receiving topical diclofenac and the other receiving ginger extract in NLC, discontinued the trial before completing evaluation of safety and efficacy. Therefore, the ITT analysis included the 118 patients (98.3% of the total enrolled). The overall dropout rate was 1.66% in two groups. The dropout rate due to adverse event was only one case in Ginger extract in NLC group and one case with loss to follow-up two times in topical diclofenac group.

Baseline demographic and clinical characteristics

The baseline characteristics of the patients

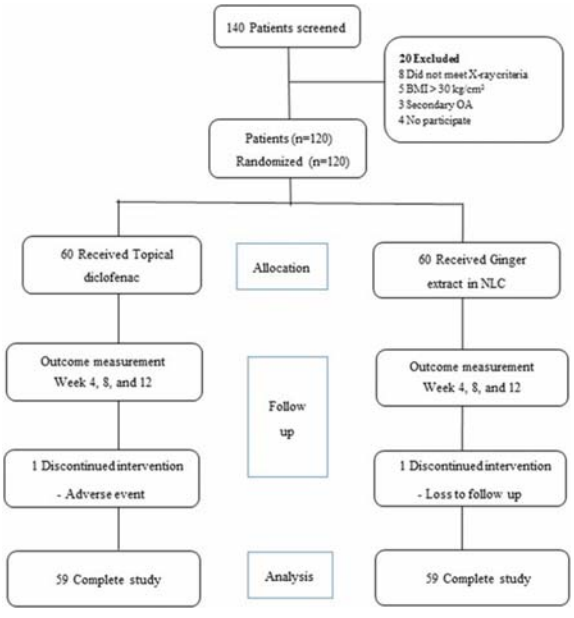

Fig. 1 Flow chart of participants.

who completed the study are shown in Table 1.

There are no differences between the two groups (Table 1).

Compliance

Compliance was calculated from the amount of study medication returned (weight of residual drugs at 4, 8, and 12-week). The mean of the Ginger extract in NLC and Topical Diclofenac used per patient were 28.8±8.7 g and 30.8±10.4 g for four weeks respectively. There was no statistical difference between the two groups by student t-test.

Clinical efficacy

The assessment of efficacy was done by the Western Ontario and McMaster Universities

Table 1. Baseline demographic, safety and efficacy characteristics of patient in the intervention and control groups

Variable	Topical diclofenac (n = 59)	Ginger extract in NLC (n = 59)	*p*-value
Sex, %			1.000[@]
Male	8 (13.5)	8 (13.5)	
Female	51 (86.4)	51 (86.4)	
Age, years, mean (SD)	61.9±6.9	61.8±6.7	0.904
Duration of disease	3.2±2.5	2.7±2.4	0.227
Body mass index, kg/m^2, mean (SD)	25.8±3.1	25.9±3.0	0.827
Heart rate, bpm, mean (SD)	78.5±10.0	76.5±3.0	0.827
Systolic blood pressure, mmHg, mean (SD)	137.2±19.5	136.2±17.1	0.765
Diastolic blood pressure, mmHg, mean (SD)	75.6±10.5	72.6±7.8	0.076
Screening index of severity for OA ([1]ISOA score 0-24), mean (SD)	11.0±4.4	10.0±3.9	0.617
Radiographic classification of knee OA, Kellgren and Lawrence x-ray, %			0.292[@]
Grade II	10 (16.9)	8 (13.6)	
Grade III	49 (83.1)	51 (86.4)	
Baseline laboratory values, (normal range) biochemical parameters			
ALP (30 to 120 U/L), mean, SD	77.0±19.6	74.6±20.6	0.517
SGOT (0 to 50 U/L), mean, SD	26.0±11.1	25.0±13.0	0.670
SGPT (0 to 45 U/L), mean, SD	31.2±16.7	27.1±16.8	0.193
BUN (5 to 23 mg/dl), mean, SD	15.7±4.5	15.8±5.8	0.944
Creatinine (0.7 to 1.3 mg/dl), mean, SD	1.2±1.3	1.0±0.2	0.271
Hematology			
White blood cell count (4.00 to 10.00x10 3/µL), mean, SD	7.8±1.9	7.7±1.7	0.748
Total RBC count (3.5 to 5.50x10 6/µL), mean, SD	4.3±0.5	4.3±0.4	0.853
Platelet count (150 to 400x10 3/µL), mean, SD	312.5±65.9	286±72.3	0.067
Hematocrit (35 to 40%), mean, SD	38.2±5.0	37.9±3.7	0.737
Baseline efficacy variable			
[1]WOMAC parameter			
Pain subscale, (score 0 to 50), mean, SD	22.3±12.0	25.4±9.0	0.124
Stiffness subscale, (score 0 to 20), mean, SD	9.3±4.9	10.0±4.4	0.475
Function subscale, (score 0 to 150), mean, SD	67.3±32.4	71.3±3.5	0.471
[3]Patient Global Assessments (PGA), (score 0 to 10), mean, SD	8.8±1.9	9.3±2.0	0.163

Student t-test, [@] Chi-square

[1]ISOA (0 = no problem, 24 = extreme severity); [2]WOMAC (0 = no knee problems, 10 = extreme knee problems); [3]PGA (10 = very poor, 0 = very good)

(WOMAC) OA composite index. The mean of WOMAC parameter of pain, stiffness, and function according to treatment group and at different visits were presented in Table 2. Each visit at 4, 8, and 12 weeks of the trial, the mean of all subscale of WOMAC were reduced from baseline in both treatment groups. In addition, the mean of WOMAC values in all the three subscales, pain, stiffens and function showed the most improvement from baseline into their therapies for both groups after 12 weeks of treatment (Fig. 2).

Mean change from baseline of pain, stiffness, physical function, and patient global assessment (PGA) on both treatment after each study visit (4, 8, and 12 weeks) were normally distributed, which was confirmed by Kolmogorov-Smimov test. Effectiveness of the treatment between baseline vs. mean change in score (at week 4, 8, and 12), showed significant improvement (p<0.05) in all WOMAC subscale and PGA in both groups. However, comparing the mean difference in change between topical diclofenac and Ginger extract in NLC group, there was no statistical difference between the two groups with repeated ANOVA (Table 3).

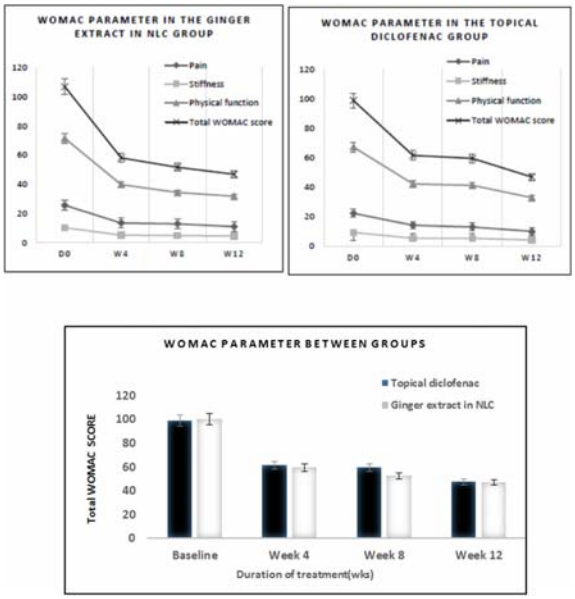

Fig. 2 The mean scores of pain, stiffness, physical function and total WOMAC score of WOMAC parameter in the Ginger extract in NLC and Topical diclofenac.

Table 2. The WOMAC parameters at baseline, 4, 8 and 12-week of Topical diclofenac and Ginger extract in NLC group

WOMAC parameter	Topical diclofenac		Ginger extract in NLC		p-value[@]
	Mean (SD)	95% CI	Mean (SD)	95% CI	
Pain					0.732
Baseline	22.2 (12.1)	19.1 to 25.4	25.4 (9.2)	22.9 to 27.9	
Week 4	14.9 (9.6)	11.4 to 16.5	13.7 (8.7)	11.3 to 16.0	
Week 8	12.8 (8.2)	10.7 to 15.0	12.9 (7.9)	10.8 to 15.0	
Week 12	10.0 (7.8)	7.9 to 12.1	10.8 (8.3)	8.6 to 13.1	
Stiffness					0.762
Baseline	9.3 (4.9)	8.0 to 10.6	10.1 (4.5)	8.5 to 11.4	
Week 4	5.2 (4.0)	4.1 to 6.3	5.1 (3.9)	4.0 to 6.1	
Week 8	5.3 (3.6)	4.4 to 6.3	4.6 (3.9)	3.6 to 5.7	
Week 12	4.1 (3.0)	3.3 to 4.9	4.3 (3.5)	3.3 to 5.3	
Function					0.417
Baseline	67.1 (32.6)	58.4 to 75.7	72.2 (27.6)	64.7 to 79.6	
Week 4	41.6 (29.6)	33.7 to 49.4	40.2 (28.5)	32.5 to 47.9	
Week 8	41.1 (26.3)	34.1 to 48.1	34.7 (24.1)	28.2 to 41.2	
Week 12	32.9 (24.7)	26.3 to 39.5	31.6 (23)	25.3 to 37.8	
Total WOMAC					0.957
Baseline	98.7 (4.7)	86.1 to 100.1	100.0 (3.8)	97.5 to 100.1	
Week 4	60.9 (4.1)	49.8 to 71.9	59.1 (3.9)	48.4 to 69.7	
Week 8	59.1 (3.6)	49.4 to 68.8	52.3 (3.4)	42.9 to 61.7	
Week 12	47.2 (3.4)	38.0 to 56.4	46.8 (3.4)	37.6 to 56.1	

p-value[@] by repeated ANOVA, Multiple comparisons: Bonferoni

The response rate for at least a 50% reduction in pain (Table 4) was significantly greater following Ginger extract in NLC treatment compared to topical diclofenac (67.7% vs. 45.7% $p<0.05$). However, a 50% improved function and 10% improved PGA was not statistically significant. Similarly, Ginger extract in NLC had non-significantly greater number of participants with OMERACT-OARSI response rate (72.8% vs. 67.7%; $p>0.05$) compared to topical diclofenac group.

Adverse events

The main adverse event reported was skin reaction at the application site, which led to discontinuation of only one participant in ginger extract in NLC who had the total score of Naranjo's algorithm +3 so a possible ADR. The adverse event appears after the suspected drug given (+1). The adverse reaction improved when the drug was discontinued (+1). However, the adverse reaction appeared when the drug was re-administered (+2) and alternative causes that could have caused the reaction (-1). However, the skin reaction resolved promptly upon withdrawal of treatment.

As a part of the safety evaluation, laboratory

Table 3. Efficacy evaluation of the mean WOMAC and patient global assessment in Ginger extract in NLC between the Topical diclofenac group by the repeated ANOVA

Efficacy variable	Treatment group, (n)	Baseline score, mean (SD)	[1]Change in score, mean (SD)	*p*-value (vs. baseline)	*p*-value (vs. topical diclofenac)
Pain (score 0 to 50)	Ginger extract in NLC (n = 59)	25.4 (12.1)	10.2 (2.9)	0.000	0.106
	Topical diclofenac (n = 59)	22.2 (9.6)	9.9 (2.8)	0.000	
Stiffness (score 0 to 20)	Ginger extract in NLC (n = 59)	10.1 (4.5)	7.1 (1.6)	0.000	0.217
	Topical diclofenac (n = 59)	9.3 (4.9)	5.7 (1.3)	0.000	
Physical function (score 0 to 150)	Ginger extract in NLC (n = 59)	72.2 (27.6)	33.3 (23.8)	0.000	0.082
	Topical diclofenac (n = 59)	67.1 (32.6)	28.5 (25.1)	0.000	
Patient global assessment (PGA) (score 1 to 10)	Ginger extract in NLC (n = 59)	9.3 (2.0)	2.5 (2.4)	0.000	0.910
	Topical diclofenac (n = 59)	8.7 (1.0)	1.6 (1.8)	0.000	

The *p*-value by repeated ANOVA, multiple comparisons: Bonferoni, 1 = comparing baseline, 2 = comparing between Topical diclofenac and Ginger extract in NLC groups

Table 4. Efficacy evaluation by OMERACT-OARSI responder

Efficacy variable	Treatment group (n)	Number (%) of participants	*p*-value[@]
50% reduction in pain	Topical diclofenac (n = 59)	27 (45.7)	0.025
	Ginger extract in NLC (n = 59)	40 (67.7)	
50% improve function	Topical diclofenac (n = 59)	27 (45.7)	0.357
	Ginger extract in NLC (n = 59)	33 (55.9)	
10% improve PGA	Topical diclofenac (n = 59)	33 (55.9)	0.255
	Ginger extract in NLC (n = 59)	40 (67.7)	
OMERACT-OARSI response	Topical diclofenac (n = 59)	40 (67.7)	0.687
	Ginger extract in NLC (n = 59)	43 (72.8)	

[@] Chi-square

tests were performed to assess different biochemical and hematological parameters. The unpaired t-test were used to compare between groups at 12 weeks Statistical analyses of these parameter did not indicate any significant change (Table 5).

Discussion

Osteoarthritis commonly affects the elderly people, and if they have associated co-morbid conditions, can lead to many treatment and include multiple medications. In these situations, giving NSAIDs will blunt the effect of antihypertensive therapy in patients with cardiovascular disease, selective COX-2 inhibitors would further increase risk of CV adverse events and NSAIDs given to patients with diabetes could increase the risk of nephropathy[4,5]. Although oral medications carry these risks, published guidelines have often recommended topical NSAIDs for treatment of OA knee[4]. Due to the above limitations, there is a need to provide alternative therapies to reduce incidence of adverse effects. In Indian and Chinese medicine, ginger has been used for time immemorial for treatment of rheumatic disorder due to its anti-inflammatory properties and ability to inhibit arachidonic acid metabolism. The active components from ginger are 6-gingerol and 6-shagaol. In animal models, ginger has been shown to act as a dual inhibitor of both cyclooxygenase (COX) and lipooxygenase (LOX)[11,12], inhibits leukotriene synthesis, and to reduce carregenan-induced rat-paw edema in animal models of inflammation. However, due to poor absorption, rapid metabolism and elimination of active compound, the bioavailability of polyphenolic compounds is poor[29]. The fact that gingerol and shogaol are insoluble in water limits its application in aqueous base systems. A study by Arunkamon[27], evaluated the anti-inflammatory activity in animal models using microemulsion formulations containing ginger extract. The ginger extract by acetone gave the highest concentration of [6]-gingerol content at 10.70 to 11.44%[29].

The present study is based on an extract of the *Zingiber officinale* rhizome which is extracted by acetone having the of [6]-gingerol content of 11.18%. Our results demonstrated ginger extract in NLC to be reducing knee pain and other symptoms, and effective in improving quality of life for 12 weeks of treatment.

The only previous study using Plygersic gel, which is a topical extract of ginger and plai (*Zingiber cassumunar* Roxb) in the ratio of about 4% by weight was used for the treatment of OA. The use of Plygersic gel has shown the ability to improve pain and other symptoms when measured by KOOS in the period of 2 to 6 weeks of treatment[28]. The present study demonstrates the potential of Ginger extract in NLC to relieve pain, joint stiffness and improving physical

Table 5. Laboratory tests at the initiation and following 12 weeks of treatments between Ginger extract in NLC and Topical diclofenac

Laboratory test	Before treatment		Treatment 12 weeks		*p*-value
	Topical diclofenac	Ginger extract in NLC	Topical diclofenac	Ginger extract in NLC	
Laboratory values, (normal range)					
Biochemical Parameters					
ALP (30 to 120 U/L) mean ± SD	77.0±19.6	74.6±20.6	77.1±18.6	77.0±20.1	0.969
SGOT (0 to 50 U/L) mean ± SD	26.0±11.1	25.0±13.0	27.4±11.2	27.0±15.0	0.870
SGPT (0 to 45 U/L), mean ± SD	31.2±16.7	27.1±16.8	38.5±16.1	40.4±20.5	0.626
BUN (5 to 23 mg/dl) mean ± SD	15.7±4.5	15.8±5.8	13.5±5.3	14.3±4.3	0.347
Creatinine (0.7 to 1.3 mg/dl) mean ± SD	1.2±1.3	1.0±0.2	1.0±0.3	1.0±0.3	0.421
Hematology					
WBC (4.00 to 10.00x10 3/µL) mean ± SD	7.8±1.9	7.7±1.7	7.3±2.0	8.0±1.9	0.080
RBC (3.5 to 5.50x10 6/µL) mean ± SD	4.3±0.5	4.3±0.4	4.4±0.4	5.0±2.7	0.323
Platelet (150 to 400x10 3/µL) mean ± SD	312.5±65.9	286±72.3	302.7±65.2	288.8±84.0	0.340
Hematocrit (35 to 40%) mean ± SD	38.2±5.0	37.9±3.7	38.3±3.6	38.1±3.7	0.684

The *p*-value by unpaired t-test compared between groups at 12 weeks

function in OA patients measured by WOMAC and the Patient Global Assessment parameters (Fig. 2, Table 3). Interestingly, Plygersic gel has demonstrated reduced pain and improved function of 27.1%, 23.4% respectively in 6 weeks[28], whereas ginger extract in NLC has shown pain reduction of 32.8% and improved function of 38.0% at 4 weeks in our current study.

The OMERACT-OARSI initiative used a consensus approach to derive dichotomous responder criteria. Through their vast meta-analysis of trials, the authors found that topical NSAIDs vs. oral NSAIDs the responder rate was 55% and 54% respectively. The strongest data was for topical diclofenac in OA of the knee the number needed to treat (NNT) for at least 50% pain relief over 8 to 12 weeks was 6.4 for NSAIDs solution and 11 for NSAIDs gel[29]. In the present study, OMERACT-OARSI responder rate was shown to be 72.8% for Ginger extract in NLC and 67.7% for topical diclofenac gel (Table 4). In addition, at least 50% reduction in pain was shown in Ginger extract in NLC group which was significantly greater than topical diclofenac gel group (67.7% vs. 45.7%). Similarly, the study by Baer et al in 2005 demonstrated 50% reduction in pain with topical diclofenac solution as 43.8% and 65.7% with OMERACT-OARSI response rate respectively[30]. However, when comparisons were made between the Ginger extract in NLC and topical diclofenac groups, OMERACT-OARSI responder rate did not shown significant differences. Safety analysis revealed no serious adverse events in clinical symptoms or laboratory test. However, minor skin reaction at the application site due to contact dermatitis was seen, which is similar to results from previous study[28].

Conclusion

Ginger extract in NLC used three times daily for 12-weeks, is as effective as 1% Diclofenac gel and it can be considered as complementary therapy in patients with osteoarthritis of knee.

What is already known on this topic?

There are interesting papers, Niempoog et al (2012) studied the efficacy of the Plysersic gel (combination of ginger and galangal) for relieving joint pain and improving problematic symptoms of OA knee. The result showed that Plysersic gel has provided for the treatment of osteoarthritis of the knee similar to the 1% Diclofenac gel group. As result of combination of ginger and plai were that ginger has strongly anti-inflammatory activity, but it has rapid metabolism and elimination of active compound, whereas galanga has prolonged anti-inflammatory activity[30].

What this study adds?

The present study has demonstrated new local application of ginger extract nanoparticles (Nanostructure lipid carriers; NLC). The requirement for formulation of a topical drug delivery system of ginger extract, which could both increase the presence of drug locally, for a prolonged period, and reduce the risk of systemic toxic. Summary, a 12-week treatment with ginger extract in NLC could relieve joint pain and improve problematic symptoms and the quality of life in knee OA patients. The topical ginger extract in NLC may be an alternative therapy in patients with osteoarthritis of knee.

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Potential conflicts of interest

None.

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การเปรียบเทียบประสิทธิผลของสารสกัดขิงนาโนกับ 1% ไดโคฟีแนคเจลในการรักษาผู้ป่วยข้อเข่าเสื่อม

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วัตถุประสงค์: เพื่อเปรียบเทียบประสิทธิผลของสารสกัดขิงนาโนกับ 1% ไดโคฟีแนคเจลในการรักษาผู้ป่วยข้อเข่าเสื่อม

วัสดุและวิธีการ: ผู้ป่วยข้อเข่าเสื่อม จำนวน 120 คน อายุระหว่างอายุ 55 ถึง 75 ปี วินิจฉัยตามหลักเกณฑ์ของวิทยาลัยแพทย์โรคข้อและรูมาติซั่มสหรัฐอเมริกา แบ่งเป็น 2 กลุ่ม สุ่มผู้ป่วยรับสารสกัดขิงนาโนหรือ 1% ไดโคฟีแนคเจลทาเข่า วันละ 3 ครั้ง เป็นเวลา 12 สัปดาห์ การประเมินประสิทธิภาพการรักษาโดยใช้ตัววัด Western Ontario and McMaster Universities (WOMAC) และ Patient's global assessment (PGA) โดยใช้สถิติ Repeated ANOVA และ Chi-square test การประเมินความปลอดภัยโลหิตวิทยาและชีวเคมีในเลือดใช้สถิติ Paired t-test เปรียบเทียบก่อนและหลังรักษา

ผลการศึกษา: สารสกัดขิงนาโนและ 1% ไดโคฟีแนคเจล ลดอาการข้อเข่าเสื่อม ลดปวดข้อเข่า เพิ่มสภาพทั่วไปกิจวัตรประจำวันและคุณภาพชีวิตของผู้ป่วยแตกต่างจากก่อนรักษาอย่างมีนัยสำคัญที่ $p<0.05$ ประเมินจากตัววัด WOMAC และ PGA นอกจากนี้พบว่าอัตราการตอบสนอง สารสกัดขิงนาโนสามารถลดปวดได้ดีกว่า 1% ไดโคฟีแนคเจลอย่างมีนัยสำคัญ และไม่พบความแตกต่างของอาการไม่พึงประสงค์ทางคลินิกและทางห้องปฏิบัติการโลหิตวิทยาหลังการรักษา

สรุป: สารสกัดขิงนาโนสามารถลดอาการปวดเพิ่มการทำงานของข้อเข่าและคุณภาพชีวิตดีขึ้นในการรักษา 12 สัปดาห์