Efficacy of Symptomatic Control of Knee Osteoarthritis with 0.0125% of Capsaicin Versus Placebo

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Background: *Knee osteoarthritis (OA) is prevalent and associated with both pain and functional disability. Current treatments aim to alleviate mild to moderate symptoms by various methods. Topical capsaicin (0.075% and 0.05%) has been evaluated for the treatment of the painful joints. A burning sensation was the most common side effect at these strengths. Therefore, the authors aimed to evaluate the efficacy of 0.0125% capsaicin gel (Capsika gel®) compared to a placebo (the vehicle gel) in patients with symptomatic OA knee.*

Material and Method: *This was a cross-over, double blinded, randomized, controlled trial of 100 patients with mild to moderate knee OA. All of the patients received either capsaicin gel or placebo gel applied to the affected knee, three times daily for 4 weeks with one week washout period after which the treatment switched to either capsaicin gel or placebo gel for the next 4 weeks. A blinded examiner used the visual analog scale (VAS) and WOMAC score to do weekly assessments.*

Results: *Subjects averaged 61 years of age (range, 44 to 82). During the enrollment phase, only female farmers presented. Mean body weight and height was 62.97 $\pm$ 10.25 kg and 1.54 $\pm$ 0.053 m, respectively. The respective baseline VAS and WOMAC score was 6.40 $\pm$ 1.64 and 51.65 $\pm$ 13.3. The severity of OA, according to the KL criteria was: 83 patients with grade 2 and 16 with grade 3.The respective mean difference of VAS and total WOMAC score in the capsaicin group vs. the placebo group was statistically significant ($p < 0.05$). The mean difference of the WOMAC pain, stiffness and functional subscales in the capsaicin vs. the placebo group was also significant ($p < 0.05$). The only adverse event reported was a burning sensation. During the 4-week treatment with capsaicin, ~67% of patients had a burning sensation but none withdrew for this reason.*

Conclusion: *0.0125% capsaicin gel was an effective treatment in mildly to moderately painful OA knees. The burning sensation reported by patients in the capsaicin group was less disturbing than in previous studies and none of the present patients withdrew for this reason.*

Keywords: *0.0125% capsaicin gel, OA knee*

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Osteoarthritis (OA) is the most common form of arthritis in the population. A recent World Health Organization report on the global burden of disease indicated that knee OA is likely to become the fourth most important global cause of disability in women and the eighth in men[1]. Knee OA is associated with symptoms of pain and functional disability. The physical disability arising from pain and loss of functional capacity reduces the quality of life and increases the risk of further morbidity and mortality[2]. Current treatments aim at alleviating the symptoms of mild to moderate OA by pharmacological and/or non-pharmacological means; evidential support, however, is mooted[3].

Capsaicin is the active principle of hot chili pepper, which may selectively stimulate unmyelinated C fiber afferent neurons and cause the release of substance P. Prolonged application of capsaicin reversibly depletes the stores of substance P and possibly other neurotransmitters, from sensory nerve endings, which reduces or abolishes the transmission of painful stimuli from the peripheral nerve fibers to the higher centers[4]. Others evaluated more potent preparations of topical capsaicin (0.075% and 0.05%) for the treatment of the painful joints of rheumatoid

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arthritis (RA) and osteoarthritis (OA) in a 4-week, double-blind, placebo-controlled, randomized trial[5-8]. In these studies, a burning sensation was the only adverse effect noted, however, none of the presented patients withdrew because of this adverse event.

Since the current treatment of OA is with NSAIDs (non-steroidal anti-inflammatory drugs) and gastrointestinal, cardiovascular and renal side effects are common. It is important to find safer pain management. Topical capsaicin would be of interest if the localized burning sensation could be mitigated. The authors, therefore, designed a study of a less concentrated preparation, capsaicin 0.0125%.

Material and Method

Subjects and study design

The authors conducted a 12-week, phase III, randomized, double-blind, placebo-controlled, cross-over trial to evaluate the efficacy of capsaicin gel over against a placebo, in adults with OA of the knee. The authors planned to enroll 100 knees (from a 100 pairs of knees). Subjects underwent 4 weeks of treatment, followed by one-week wash-out, then another 4 weeks of treatment. The authors alternated the treatment after one-week wash-out.

The Khon Kaen University Ethics Committee for Human Research approved the study in accordance with the Helsinki Declaration. All of the subjects gave informed consent.

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The registration number for the research is: Clinical Trials. gov ID NCT00471055.

Inclusion and exclusion criteria

The inclusion criteria:

1. Capable of giving written informed consent;
2. Ambulatory males, or non-pregnant females, between 40 and 80 years of age;
3. Off pain medication or nutritional supplements for symptomatic relief of knee OA at least 15 days before screening;
4. Pain in the knee $\leq$ 80 mm on a 100 mm VAS scale;
5. Have a diagnosis of OA of the knee at least 6 months prior to screening, or have met the American College of Rheumatology (ACR) clinical criteria for classification of idiopathic (primary) OA. (If OA presents in both knees, the investigator will X-ray for study entry the knee with more severe pain ($\leq$ 80 mm VAS).
6. Present documented radiographic evidence of OA of the knee (from the screening visit radiograph) of grade 2 or 3 on the Kellgren and Lawrence (KL) Radiographic Grading[9]; and
7. A baseline minimum joint space width in the medial and lateral compartments of the index knee of $\geq$ 1.5 and $\geq$ 2.5 mm, respectively, measured from radiographs in the MTP view[10].

The exclusion criteria:

1. History of hypersensitivity to capsaicin;
2. Skin lesion at the index (treated) knee;
3. A history of lower extremity surgery within 6 months prior to screening;
4. Significant prior injury to the index knee within 12 months prior to screening;
5. Disease of the spine or other lower extremity joints of sufficient degree to affect the index knee; and
6. Treatment with other drugs potentially affecting bone or cartilage metabolism, such as:
   - Chronic systematic corticosteroids;
   - Hyaluronan injection into the index knee within the previous 6 months; and
   - Diacerin treatment within the last 12 months.

Study protocol

The authors conducted a cross-over, randomized, controlled trial, in which subjects were randomly allocated to study-arms, where each arm comprised a sequence of two treatments given consecutively ($A^{capsaicin}$ then $B^{placebo}$ or B then A). Subjects allocated to the AB study arm of the study received 4 weeks of treatment $A^{capsaicin}$ followed by a one-week wash-out then another 4 weeks of treatment $B^{placebo}$. The reversed pattern was followed in arm BA. With this protocol, any lasting effects of the capsaicin should be differentiable from the placebo effect. Each subject received either Capsaicin or placebo gel, according to a randomization schedule, stratified by KL grade 2 or 3.

The authors provided capsicum tincture 45.50 g (equivalent to capsaicin 0.0125%) per 100 g of Capsika gel® in a lacquered aluminum collapsible tube containing 100 g Gel packing. Subjects applied 2 inches of extruded gel topically around the index knee and rubbed it in until dry for three times a day. After applying the gel, patients were to wash their hands, to avoid eye irritation.

The returned gel was weighed, providing a measure of compliance. The subjects kept a treatment diary, including: (1) the number of doses of gel applied each day; and, (2) any (or change in any) other

concomitant therapy during the study, including pain medication or nutritional supplements for OA related pain. Subjects were permitted to take acetaminophen for pain-500 mg three times a day (or every 4-6 hours)-but not any other topical analgesics, NSAID or COX-2 inhibitors. They worked as per usual and the authors did not provide any knee brace or physical therapy.

Wash-out

If subjects took acetaminophen for OA pain during the 7-day wash-out, they were to record how much.

End points and statistics

The authors aimed to determine whether capsaicin gel could reduce pain (VAS)-the functional score and the stiffness score-over against the placebo gel. The authors hypothesized that capsaicin gel would reduce the VAS by 50%. Therefore, the primary endpoint was any change from the baseline of the visual analog scale (VAS), corroborated by any change in the Western Ontario McMaster score (WOMAC). The authors measured these endpoints every week for 9 weeks (*i.e.,* 4 weeks for each treatment period and one week for the wash-out).

The calculated sample size was 96 knees, based on: (1) a mean difference of VAS of 30 mm; (2) a standard deviation of 60 mm; (3) a 95% (alpha 5%) significance level for a two-sided test; and, (4) 80% (beta 20%) power for detecting a difference[10]. Assuming a 5% dropout rate, the authors needed to enroll 100 knees for each treatment group.

The Z test (at a 95% CI) assessed the mean difference of VAS in the Capsaicin and placebo group. The ANOVA, student t-test and McNemar's Chi-square tested the difference between baseline and post-treatment for WOMAC, Stiffness score and acetaminophen use, respectively (Stata Corp. 2007. Stata Statistical Software: Release 10. College Station, TX: SataCorp.). A P-value of less than 0'05 was considered significant.

Results

Between July and October, 2007, the authors registered 100 female cases, diagnosed with osteo-arthritis of the knee joints. One case dropped out. The mean age was 61 years (range, 44-82). The affected knee joints enrolled in the present study included 54 right knees and 45 left knees. The respective mean medial joint space width of the right and left knees was 0.355 ± 0.195 and 0.346 ± 0.216 cm (Table 1).

The mean body weight and height was 62.97 ± 10.25 kg and 1.54 ± 0.053 m. The respective baseline VAS and WOMAC score was 6.40 ± 1.64 and 51.65 ± 13.30. The severity of OA as per the KL criteria was grade 2 in 84 patients and grade 3 in 16 patients (Table 1).

The capsaicin remaining in the returned tube averaged 38.07 ± 12.46 g in the capsaicin group and 41.48 ± 14.35 g in the placebo group ($p > 0.05$).

The mean reduction in VAS from the baseline and wash-out period was significantly greater in the Capsaicin group than in the Placebo group ($p < 0.05$) (Tables 2, 3). The mean VAS in the wash-out period in both groups was less than the mean baseline VAS; albeit the difference was not statistically significant ($p > 0.05$).

The reduction in the standardized mean WOMAC score from baseline and wash-out was significantly greater in the Capsaicin group than in the placebo group ($p < 0.001$) (Table 4). The mean WOMAC scores in the wash-out period were also reduced in

Table 1. Clinical characteristics of the study population at the baseline

Sex (female to male ratio)	99:0
Age (years) (min-max)	61 (44-82)
Affected knees, ratio of right to left knees	54:45
Mean, weight : height	62.97 ± 10.25 kg and 1.54 ± 0.053 m
Medial Joint space (cm), ratio of right to left	0.35 ± 0.19 (0-0.7): 0.35 ± 0.26 (0-0.8)
Lateral Joint space (cm), ratio of right to left	0.54 ± 0.21 (0-1.5): 0.58 ± 0.17 (0-1.1)
VAS	6.40 ± 1.64 (3-10)
WOMAC score	51.65 ± 13.30 (44-76)
Pain subscale	11.09 ± 3.06 (5-16)
Stiffness score subscale	2.81 ± 2.45 (0-8)
Functional score subscale	38.92 ± 9.89 (17-57)
KL grading, ratio of grade 2 to 3	84:16

Table 2. Means and standard deviations of VAS at pre-treatment, washout and post-treatment in the capsaicin and placebo groups

Treatment	V0	V1*	V2*	V3*	V4*	V5	Treatment	V6**	V7**	V8**	V9**
Capsaicin n = 65	6.27 ± 1.78	6.41 ± 1.77	5.27 ± 1.49	5.04 ± 1.33	4.46 ± 1.46	4.60 ± 1.37	Placebo n = 65	4.18 ± 1.40	4.17 ± 1.14	3.93 ± 1.33	3.69 ± 1.59
Placebo n = 34	6.64 ± 1.35	7.67 ± 1.07	6.21 ± 1.23	5.51 ± 1.19	4.56 ± 1.35	4.50 ± 1.21	Capsaicin n = 34	4.00 ± 1.61	3.53 ± 1.08	3.18 ± 1.75	2.03 ± 1.68

ANOVA * V0 vs. V1-4 in the capsaicin group were less than the placebo group ($p < 0.002$)
ANOVA ** V5 vs. V6-9 in the capsaicin group were less than the placebo group ($p < 0.002$)
V5 was the washout period

Table 3. Comparing the mean difference of VAS from baseline and each visit in the capsaicin and placebo groups

Visit	Capsaicin mean ± SD n = 99	Placebo mean ± SD n = 99	Mean different mean ± SE	95% CI
1	0.08 ± 1.79	0.08 ± 1.58	0.16 ± 0.24	-0.31 to 0.63
2	0.98 ± 1.80	0.42 ± 1.45	0.56 ± 0.23	0.10 to 1.02
3	1.26 ± 1.94	0.82 ± 1.61	0.43 ± 0.25	0.06 to 0.93
4	2.04 ± 1.93	1.31 ± 1.97	0.72 ± 0.27	0.17 to 1.27

both groups but the differences were not statistically significant ($p > 0.05$).

The mean reduction of the total and three WOMAC subscales (*viz.,* the pain, stiffness and functional scales) from baseline and wash-out periods were also significantly lower in the Capsaicin group than in the Placebo group ($p < 0.05$) (Tables 5-8).

The average amount of acetaminophen used in the Capsaicin group was 6.06 ± 6.38 tablets per week (range, 0-21; median, 4) versus 4.98 ± 4.72 tablets per week (range, 0-21; median, 3) in the placebo group; the differences were not statistically significant ($p > 0.05$).

A burning sensation was the only adverse event reported in our study: *viz.,* 66 episodes over a 4-week period (16.6%) in the placebo group vs. 272 episodes (66.66%) in the capsaicin group. A burning sensation during both the capsaicin and placebo periods was reported by 34 patients (34.34%). By comparison, 57 patients (57.58%) had a burning sensation only during the capsaicin period ($p < 0.05$). None of the presented patients withdrew because of this adverse event.

Discussion

The authors conducted a double-blinded, randomized, placebo, cross-over, controlled trial for treatment of OA of the knee. Since OA is a chronic stable disease, self-comparison of each subject is possible and other confounders can be controlled.

Characteristics of the medication dispensing tube and the color of the capsaicin and placebo gels were the same; thus, neither the patients nor the examiner could know whether the patient was in the capsaicin or the placebo group. In addition, any measurement bias was controlled by use of the double-blinded method.

All of the patients were farmers and females, most of them still working, which reflects the real

Table 4. Means and SDs for WOMAC at pre-treatment, washout (V5) and post-treatment in the capsaicin and placebo gel groups

Treatment	V0	V1*	V2**	V3**	V4**	V5	Treatment	V6*	V7**	V8**	V9**
Capsaicin n = 65	53.14±13.93	38.71±20.04	36.23±19.94	34.77±20.47	32.15±19.22	33.60±19.87	Placebo n = 65	34.78±21.02	33.65±19.38	32.34±19.27	30.66±19.25
Placebo n = 34	49.03±11.66	34.68±16.93	37.35±18.25	35.24±14.92	34.79±14.99	31.47±16.92	Capsaicin n = 34	23.00±15.47	19.88±13.64	16.56±11.85	13.21±10.75

ANOVA* V0 vs. V1 and V5 vs. V6 in the capsaicin group were not different from the placebo group ($p > 0.05$)
ANOVA** V0 vs. V2-4 and V5 vs. V7-9 in the capsaicin group were less than the placebo group ($p < 0.02$)
V5 was a washout period

Table 5. Comparing the mean difference for the WOMAC score from baseline and each visit in the capsaicin and the placebo groups

Visit	Capsaicin mean ± SD n = 99	Placebo mean ± SD n = 99	Mean different mean ± SE	95% CI
1	3.27 ± 4.30	0.40 ± 3.14	2.86 ± 0.53	1.81 to 3.92
2	3.78 ± 3.85	0.62 ± 3.75	3.16 ± 0.54	2.09 to 4.23
3	4.13 ± 4.22	0.98 ± 3.24	3.15 ± 0.53	2.09 to 4.21
4	4.67 ± 4.14	1.24 ± 3.55	3.42 ± 0.55	2.34 to 4.51

Table 6. Comparing the mean difference for the WOMAC score (pain subscale) from baseline at each visit in the capsaicin and the placebo groups

Visit	Capsaicin mean ± SD n = 99	Placebo mean ± SD n = 99	Mean different mean ± SE	95% CI
1	3.27 ± 4.30	0.40 ± 3.14	2.86 ± 0.53	1.81 to 3.92
2	3.78 ± 3.85	0.62 ± 3.75	3.16 ± 0.54	2.09 to 4.22
3	4.13 ± 4.21	0.97 ± 3.23	3.15 ± 0.53	2.09 to 4.20
4	4.66 ± 4.14	1.24 ± 3.55	3.42 ± 0.54	2.34 to 4.50

Table 7. Comparing the mean difference of the stiffness subscale of WOMAC from baseline and each visit in the capsaicin and the placebo groups

Visit	Capsaicin mean ± SD n = 99	Placebo mean ± SD n = 99	Mean different mean ± SE	95% CI
1	0.50 ± 2.56	0.23 ± 1.78	0.73 ± 0.31	0.11 to 1.35
2	0.70 ± 2.41	0.09 ± 1.73	0.79 ± 0.29	0.20 to 1.38
3	0.56 ± 2.20	0 ± 2.03	0.56 ± 0.30	0.02 to 1.15
4	0.83 ± 2.40	0.11 ± 2.10	0.82 ± 0.32	0.19 to 1.46

Table 8. Comparing the mean difference of the functional subscale of the WOMAC score from baseline and each visit in the capsaicin and placebo groups

Visit	Capsaicin mean ± SD n = 99	Placebo mean ± SD n = 99	Mean different mean ± SE	95% CI
1	8.60 ± 14.24	2.60 ± 10.70	6.00 ± 1.79	2.46 to 9.53
2	10.58 ± 13.09	3.44 ± 10.34	7.14 ± 1.67	3.83 to 10.44
3	12.48 ± 13.70	4.58 ± 10.26	7.89 ± 1.72	4.50 to 11.29
4	14.54 ± 13.62	5.56 ± 10.79	8.97 ± 1.74	5.53 to 12.42

situation of OA of the knee in rural, Northeast Thailand. In the present study, the severity of OA ranged from mild to moderate or KL Grade 2 to 3.

One week before starting the study, all of the patients learned how to apply the gel topically. The amount (weight) of capsaicin and placebo remaining in the returned tubes would provide a measure of compliance. As such, the authors found patients complied with the treatment notwithstanding the *au courant* treatment group.

The present study indicates that capsaicin gel 0.0125% applied three times daily provided significantly better pain relief than the placebo gel (Table 2). The greater reduction in the mean WOMAC scores in the capsaicin group over against the placebo group support the conclusion (Table 4). Patients in the placebo group also experienced a lowering of their pain, as in other studies on the treatment of OA knee[12]. The present study, however, showed that capsaicin had a longer duration of action than one week, perhaps because patients who applied the placebo gel after the capsaicin gel might have experienced a carry-over effect in the second period to a greater extent than those who applied capsaicin gel after the placebo gel. Such reasoning is borne out by similar studies showing that repeated topical capsaicin application transiently increases the noxious heat threshold and reduces the neurogenic vascular reaction and that both the nociceptive afferent and local regulatory efferent function of the capsaicin-sensitive fibers recovers weeks after cessation of treatment[13-16].

The pain reduction in the capsaicin period was consistently greater than in the placebo period for each patient. Specifically, the VAS and WOMAC scores showed greater improvement in the capsaicin group than in the placebo group, possibly due to reversible depletion of stores of substance P (SP), and other neurotransmitters, from sensory nerve endings.

Many studies show that sensory innervation of the joint-*by capsaicin-sensitive primary afferent neurons*-is not only involved in sensory input for stretch and pain, but also has local and systemic effector functions[17,18]. Neuropeptides-*released from these fibers into the surrounding tissues*-elicit neurogenic inflammation around the site of activation. Substance P releases inflammatory mediators from mast cells, which induces the secretion of prostaglandin E2 and collagenase from synoviocytes and interleukin-1 (IL-1) from macrophages[19].

Increased levels of pro-inflammatory sensory neuropeptides, (*i.e.,* bradykinin, lipoxygenase enzyme products, prostaglandins) are present in the synovial fluid taken from patients with rheumatoid arthritis[20] and from arthritic experimental animals[21]. It has been suggested that SP constitutes the most important neurogenic mediator in the inflammatory process and that it participates in the nociceptive pathway[22].

In the present study, local adverse events of 0.0125% capsaicin gel were found more frequently in the capsaicin group as with previous studies[6-8]; however, none of the present patients withdrew from the study due to this burning sensation. Thus, capsaicin 0.0125% is well tolerated. The generalizability of the present study, however, is limited because only females enrolled. A follow-on trial that includes men needs to be designed.

The authors conclude that capsaicin cream 0.0125% (Capsika gel□) applied three times daily for treatment of mild to moderately painful OA knees provides significantly more pain relief than the placebo after four weeks of capsaicin treatment. OA knee patients demonstrated significant mean reductions of their VAS and WOMAC scores compared to the placebo. A burning sensation was reported more frequently in the capsaicin group, but there was lack of compliance due to this concern.

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ประสิทธิผลด้านการควบคุมอาการข้อเข่าเสื่อมด้วยยาแคปไซซิน 0.0125% เปรียบเทียบกับยาหลอก

วีระชัย โควสุวรรณ, วินัย ศิริชาติวาปี, ทวีโชค วิษณุโยธิน, ผลศักดิ์ จีรวิพลูวรรณ, วิรุฬห์ เหล่าภัทรเกษม

***ภูมิหลัง**: ข้อเข่าเสื่อมที่มีอาการปวดและทำให้ความสามารถในการทำงานลดลงพบได้บ่อย เป้าประสงค์ในการรักษาปัจจุบันคือ การลดอาการปวดขนาดปานกลางและปวดมาก ยาทาแคปไซซิน (0.075% และ 0.05%) ได้รับการประเมินว่าสามารถรักษาอาการปวดของข้อต่าง ๆ แต่ปัญหาที่พบคือแสบร้อนที่บริเวณที่ทายา การศึกษาในครั้งนี้เพื่อประเมินประสิทธิผลของยาทาแคปไซซินขนาด 0.0125% (Capsika gel) เปรียบเทียบกับยาหลอกในผู้ป่วยข้อเข่าเสื่อมที่มีอาการ*

***วัสดุและวิธีการ**: เป็นการศึกษาเชิงทดลองแบบสุ่ม cross-over, double blinded ในผู้ป่วยจำนวน 100 คน ที่มีความรุนแรงของข้อเข่าเสื่อมขนาดเล็กน้อยถึงปานกลาง ผู้ป่วยทุกคนจะได้รับยาทาแคปไซซินหรือยาหลอก 4 สัปดาห์แรก แล้วหยุดยา 1 สัปดาห์ ต่อจากนั้นสลับยาที่เคยได้ยาหลอกจะได้ยาแคปไซซินหรือจากได้ยาแคปไซซิน จะเปลี่ยน มาได้ยาหลอกแทน 4 สัปดาห์ ผู้ป่วยจะได้รับการประเมินความเจ็บปวด (VAS) และคะแนน WOMAC ทุกสัปดาห์ โดยผู้ประเมินและผู้ป่วยไม่ทราบว่าผู้ป่วยได้รับยาแคปไซซินหรือยาหลอก*

***ผลการศึกษา**: ผู้ป่วยมีอายุเฉลี่ยที่ 61 ปี (ช่วงอายุ 44-82 ปี) เป็นหญิงชาวนาทั้งหมด มีน้ำหนักและความสูงเฉลี่ยเท่ากับ 62.97 $\pm$ 10.25 กิโลกรัมและ 1.54 $\pm$ 0.05 เมตรตามลำดับค่า VAS และคะแนน WOMAC ก่อนการรักษาเท่ากับ 6.40 $\pm$ 1.64 และ 51.65 $\pm$ 13.3 ตามลำดับ ระดับความรุนแรงของข้อเสื่อมตามเกณฑ์ของ KL เกรด 2 จำนวน 83 คน และเกรด 3 จำนวน 16 คน ค่าเฉลี่ยของ VAS และคะแนน WOMAC เปลี่ยนแปลงดีขึ้นในผู้ป่วยที่ใช้ยาแคปไซซินมากกว่าในผู้ป่วยที่ได้รับยาหลอกอย่างมีนัยสำคัญ ($p < 0.05$) ค่าเฉลี่ยของคะแนน WOMAC ในคะแนนย่อย pain, stiffness และ function subscales ที่เปลี่ยนแปลงดีขึ้นพบมากในผู้ป่วยที่ได้รับยาแคปไซซิน มากกว่าผู้ป่วยที่ได้รับยาหลอกอย่างมีนัยสำคัญ ($p < 0.05$) อาการข้างเคียงที่ตรวจพบมีเพียงอย่างเดียวคือ อาการแสบร้อนที่ผิวหนังบริเวณที่ทายาในช่วง 4 สัปดาห์ ที่ทายาแคปไซซินและยาหลอกโดยพบร้อยละ 67 ในกลุ่มแคปไซซิน อย่างไรก็ตามไม่มีผู้ป่วยขอถอนตัวจากการศึกษา ด้วยเหตุผลนี้*

***สรุป**: ยาทาแคปไซซิน 0.0125% มีประสิทธิผลในการลดอาการของผู้ป่วยข้อเข่าเสื่อม ที่มีความรุนแรงเล็กน้อยถึงปานกลาง ผู้ป่วยรายงานอาการแสบร้อนที่ผิวหนังน้อยกว่าการศึกษาอื่น ๆ และไม่มีการถอนตัวจากการศึกษาด้วยเหตุผลดังกล่าว*