



# Effect of ThermaCare HeatWraps and Icy Hot Cream/Patches on Skin and Quadriceps Muscle Temperature and Blood Flow



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## Abstract

**Objectives:** The purpose of this study was to compare the effects of over-the-counter treatments—ThermaCare HeatWraps (chemical reaction to produce heat above the skin), Icy Hot Patch, and Icy Hot Cream (topically applied menthol)—on skin and deep tissue temperature.

**Methods:** This was a longitudinal crossover study. On each of 3 days, a ThermaCare HeatWrap, Icy Hot Cream, or Icy Hot Patch was applied randomly over the quadriceps muscle in 15 healthy volunteers with normal body mass. Skin and muscle temperature and blood flow were measured by laser flowmetry every 15 minutes for 2 hours.

**Results:** After 2 hours, mean temperature decreased by 2.1°C (7.0%;  $P = .02$ ) in skin and 1.0°C (2.9%;  $P = .01$ ) in muscle with Icy Hot Cream. Icy Hot Patch decreased skin and muscle temperature by 1.7°C (5.4%;  $P = .03$ ) and 1.3°C (3.8%;  $P = .01$ ), respectively. In contrast, ThermaCare raised skin and muscle temperature by 7.8°C (25.8%;  $P = .001$ ) and 2.7°C (7.7%;  $P = .002$ ), respectively; both were significantly warmer with ThermaCare vs either Icy Hot product (all  $P < .007$ ). Icy Hot products produced a net decrease in skin blood flow (Cream: 56.7 flux [39.3%;  $P = .003$ ]; Patch: 19.1 flux [16.7%;  $P = .045$ ]). Muscle blood flow decreased with

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the Patch (6.7 flux [7.0%;  $P = .02$ ]). After a period of fluctuations, Icy Hot Cream produced a net increase vs baseline of 7.0 flux (16.9%;  $P = .02$ ). ThermaCare more than doubled blood flow in skin (83.3 flux [109.7%;  $P = .0003$ ]) and muscle (25.1 flux [148.5%;  $P = .004$ ]).

**Conclusions:** In this group of 15 healthy volunteers, ThermaCare HeatWraps provided the greatest degree of tissue warming and increase in tissue blood flow.

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## Introduction

Dull, diffuse muscle pain that occurs after unaccustomed exercise is a well-recognized clinical phenomenon known as *delayed-onset muscle soreness* (DOMS).<sup>1</sup> Delayed-onset muscle soreness is particularly common in sedentary individuals who have initiated a new exercise program, but it can also occur in athletes who have acutely intensified their level of exercise. Delayed-onset muscle soreness–related pain typically begins about 8–10 hours after intense exercise and peaks at 24–72 hours.<sup>1–3</sup> Delayed-onset muscle soreness–related pain may be accompanied by muscle stiffness, tenderness to palpation or movement, reduced mobility/flexibility, and decreased muscle strength.<sup>1,3</sup> The pain and soreness typically subside within 5–7 days of the initial insult,<sup>3</sup> but associated muscle weakness may persist for up to 2 weeks.<sup>1</sup>

An optimal therapeutic strategy for relief of DOMS would be one that provides analgesia while promoting healing of damaged muscle tissue. Although many DOMS mechanisms have been proposed (lactic acid accumulation,<sup>3,4</sup> muscle spasm,<sup>4,5</sup> connective tissue<sup>4,6</sup> or muscle damage,<sup>4,7,8</sup> enzyme shifts,<sup>4,9,10</sup> inflammation,<sup>4,7,11</sup> production of reactive oxygen species<sup>12</sup>), most are controversial or refuted.<sup>4,13</sup> However, muscle damage leading to DOMS remains a viable theory.<sup>4</sup> Intense exercise has been associated with elevated plasma concentrations of various biomarkers indicative of stress or muscle damage (eg, heat shock proteins 27 and 70, lactate dehydrogenase, creatinine phosphokinase, and myoglobin).<sup>14–17</sup>

Both topical and deep heat modalities have been shown to reduce pain associated with DOMS.<sup>18</sup> Although untreated DOMS is reduced considerably 72 hours after exercise with an active warm-down,<sup>19</sup> heat application provides faster relief of symptoms. In subjects with moderate DOMS, Mayer et al<sup>20</sup> found that low-level heat wraps resulted in significantly greater pain relief 24 hours postexercise in comparison with cryotherapy using a standard gel-filled cold pack ( $P = .026$ ). As an extension of these findings, we have

previously reported that applying low-level heat wraps for 8 hours immediately after exercise reduces muscle soreness observed at 24 and 48 hours.<sup>21</sup>

Various “heat products” are available over the counter (OTC) that promise to provide pain relief for conditions such as DOMS. What is not readily known, however, is the degree to which these options transfer heat to tissues and increase blood flow, which is a parameter that is relevant to the process of tissue healing. ThermaCare HeatWraps, Icy Hot Patches, and Icy Hot Cream are examples of OTC products that promise to relieve pain.

ThermaCare HeatWraps are lightweight, air-activated, single-use products that deliver continuous, low-level, dry heat reaching 40°C within 30 minutes of application.<sup>22,23</sup> ThermaCare HeatWraps have previously been shown to result in deep heating of tissues.<sup>20,24,25</sup> Icy Hot Patches contain 5% menthol, and Icy Hot Cream contains 10% menthol.<sup>26,27</sup> Less is known about the effects of Icy Hot products on temperature or blood flow in skin and muscle tissue. It is possible that menthol could have an insulating effect on tissue, reducing heat loss through the skin and resulting in warming. However, it is also plausible that evaporation of menthol would cool the skin, which might induce the hunting response (ie, intermittent periods of vasodilation lasting 5–10 minutes followed by vasoconstriction and then alternating periods of each).<sup>28</sup> It is also unknown whether the menthol from these products penetrates deep enough to interact with menthol-sensitive transient receptor potential (TRP) receptors in muscle tissue. In addition to menthol, Icy Hot Cream contains methyl salicylate 30%,<sup>27</sup> a prostaglandin inhibitor. Methyl salicylate may contribute to effects on blood flow. For example, it has been reported that an analgesic balm containing methyl salicylate and capsaicin applied to the forearm skin attenuated muscle-contraction–induced increases in blood pressure.<sup>29</sup>

Although all 3 types of products are sold over the counter and used commonly, a head-to-head comparison of the effects of the 3 types of products on skin and muscle temperature and blood flow has not been made. Although a head-to-head comparison in DOMS is also

needed, DOMS in itself alters blood flow and muscle temperature.<sup>30</sup> Therefore, to eliminate this variable, only noninjured subjects were examined here. The hypothesis to be tested was that continuous low-level heat (ThermaCare) would provide faster changes in deep tissue temperature than the other 2 products. The purpose of this investigation was to assess the physiologic effects of 3 popular OTC topical analgesic products, ThermaCare HeatWraps, Icy Hot Patches, and Icy Hot Cream, for their ability to increase temperature and blood flow in both skin and muscle.

## Methods

### Study Participants

Healthy adult men and women aged 20–40 years with a body mass index of 15–25 kg/m<sup>2</sup> were eligible for study inclusion. Subjects were recruited by flyer to students, staff, and faculty at Loma Linda University or Azusa Pacific University in spring of 2012. Exclusion criteria included known peripheral cardiovascular disease or circulatory impairment (eg, Raynaud disease), presence of neurologic or orthopedic injuries, use of alpha or beta agonists or antagonists, use of any other medication that could potentially alter blood pressure or blood flow, sensitivity to heat or cold, and blood pressure >145/90 mm Hg or <90/50 mm Hg. All protocols and procedures were approved by the Institutional Review Boards of Loma Linda University or Azusa Pacific University, and all participants provided written informed consent prior to any study procedures. This study was supported by an executed investigator-initiated agreement with Wyeth Pharmaceuticals, which was acquired by Pfizer Pharmaceuticals in October 2009.

### Procedures

On each of 3 different days, participants entered a 22°C room and sat for 20 minutes to acclimate. Skin over the belly of the quadriceps muscle was then sterilized, and skin and muscle probes were placed as detailed below. All probes were placed 1 cm apart on the skin surface.

Skin temperature was measured using a single thermocouple (Model TX-4 Skin Surface Probe; Columbus Instruments, Columbus, OH) plugged into an IsoThermix thermocouple conditioner. Skin temperature was also measured with a thermal camera (FLIR infrared imager, model 670; FLIR Systems, Wilsonville, OR). A single skin temperature sensor was used to calibrate the

emissivity of the camera such that temperatures measured with the camera were validated.

Deep muscle temperature was measured with a type T thermocouple probe (IT-18; Physiotemp Instruments, Clifton, NJ). This device, which consists of a 24-gauge thermocouple with a time constant of 0.3 second, was placed into the barrel of a 21-gauge needle and inserted 2.5 cm into the quadriceps muscle under sterile conditions. Position and depth were confirmed by ultrasonography, and the needle was removed, leaving the thermocouple catheter in place for the duration of the 2-hour study period. Its output was transduced by an IsoThermix digital thermometer system (Columbus Instruments). The device is accurate to 0.1% and is medically rated with proper radiofrequency isolation to minimize risk to subjects.

Tympanic temperature was measured using an infrared thermometer (Braun Thermoscan Type 6022; Braun GmbH, Kronberg, Germany) as an assessment of central core temperature.

Skin blood flow was recorded at 6 sites around the belly of the quadriceps muscle at each time point using an infrared laser Doppler flowmeter, and an average of the 6 results was calculated. The meter has a flat 3-g probe with an active surface area of 1 cm<sup>2</sup> (TSD140 probe; BIOPAC Systems, Goleta, CA), which samples 1 mm<sup>3</sup> of tissue. The probe was connected to an amplifier (LDF100C, BIOPAC Systems), and signals were digitized at a rate of 2000 samples per second through a 24-bit analog-to-digital converter (biopac mp150, BIOPAC Systems). The unit was warmed for 30 minutes before flow measurements, and the flow probe was calibrated prior to and at the end of each series of experiments.

Muscle blood flow was measured by a laser Doppler flowmeter (produced by Moor Instruments, Oxford, England, and marketed by BIOPAC Systems). A fiber-optic plastic catheter was delivered to deep muscle tissue through the barrel of a 21-gauge needle under sterile conditions, as described for the thermocouple probe. An infrared laser probe emitting a very low level beam through the fiber-optic catheter was then used to sample blood flow in a 1-mm<sup>2</sup> area. The amplifier and digital converter described above for skin blood flow also were used in the muscle blood flow measurements.

### Treatments Administered

Following placement of the thermocouples and blood flow probes, 1 of 3 OTC products designed for relief of muscle pain was placed or applied to the skin over the belly of the quadriceps muscle: ThermaCare HeatWraps (Pfizer Consumer Healthcare, Madison,

NJ), Icy Hot Cream (Chattem, Chattanooga, TN), and Icy Hot Patches (Chattem).

ThermaCare HeatWraps produce a chemical dry heat resulting from an iron oxidation reaction. We applied the wraps over the quadriceps muscle so that the center of the wrap was immediately over both needle insertion points.

Icy Hot Patches contain 5% menthol ointment in a breathable cotton transdermal pad. More than one 10 × 20-cm Patch was applied to achieve a site of contact the same size as that of the ThermaCare HeatWrap. Because Icy Hot products are contraindicated for application over a wound, the catheter insertion sites were sealed with collodion, and a hole 1 cm in diameter was cut in the center of the Patch and placed around the catheter insertion points.

Icy Hot Cream containing 10% menthol and 30% methyl salicylate was rubbed into the skin in a thin layer for 1 minute in an area equivalent to that covered by the ThermaCare HeatWrap. No Cream was applied within 0.5 cm of the catheter insertion sites.

Each participant received all 3 treatments in a random sequence based on a statistical table. Treatments were administered open label, 1 each on 3 separate days separated by a period of 1 day between treatments.

## Outcome Measures

Temperature and blood flow were recorded continuously for muscle tissue and analyzed at 15-minute intervals during the first 2 hours after application. Skin measurements were made every 30 minutes to allow for momentary removal of the heat wraps; data for the intervening 15-minute intervals were interpolated by averaging the data from the prior and succeeding times. Thermal images were made at the time of product application and at 30-minute intervals for 2 hours thereafter.

## Data Analysis

G\*Power 3.1.9.2 software was used to calculate the sample size that would be likely to detect an effect size of 0.8 between the 2 dependent means (matched pairs). Based on this software calculation, a sample size of 15 would provide 82% power to detect statistically significant differences between products at the  $\alpha = 0.05$  level of significance. Means and standard deviations (SDs) were calculated for skin and muscle temperature and blood flow at each time point. Changes in these values from baseline to 2 hours were assessed for statistical significance using analysis of variance and *t* tests, with the threshold for statistical significance

defined as  $P < .05$ . For each outcome measure at the conclusion of the assessment period, pairwise comparisons of ThermaCare HeatWraps vs each of the Icy Hot products were performed using Fisher exact test, with a threshold for statistical significance of  $P < .05$ .

## Results

### Subject Disposition and Baseline Demographics

Fifteen healthy volunteers, 12 men and 3 women, were enrolled in the study and completed assessments with all 3 treatments. The mean (SD) age of subjects was 26.8 (4.1) years, height was 174.1 (13.5) cm, weight was 84.2 (20.1) kg, and body mass index was 27.7 (11.4).

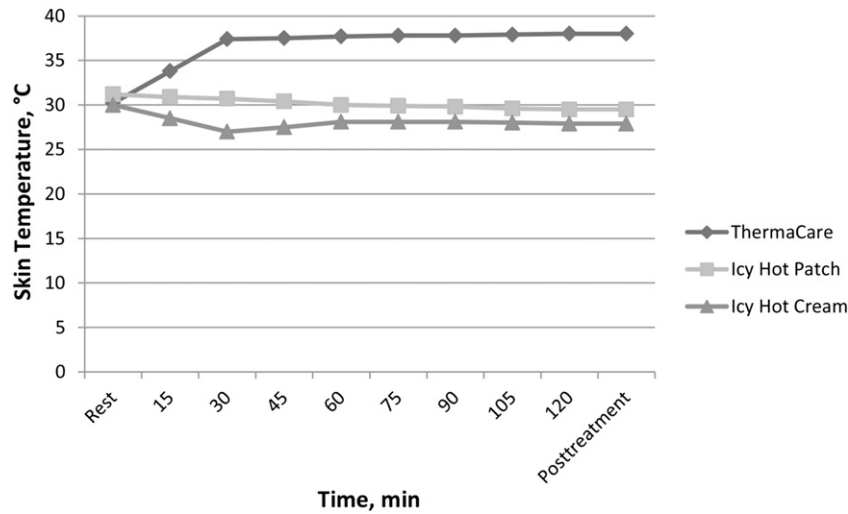
### Skin Temperature

Both Icy Hot products resulted in a modest net decrease in skin temperature over the 2-hour study period (Fig 1). With Icy Hot Cream, baseline mean (SD) skin temperature was 30.0°C (0.6°C). Mean (SD) skin temperature decreased to 27.0°C (0.7°C) at 30 minutes and then rose slightly and plateaued at approximately 28.0°C (0.6°C) for the remainder of the assessment period. The change from baseline of -2.1°C (-7.0%) was statistically significant ( $P = .02$ ). Similarly, Icy Hot Patch produced a change from baseline of about -1.7°C (-5.4%) over the 2-hour evaluation period,  $P = .03$ , which was no different than for Icy Hot Cream ( $P = .12$ ).

In contrast, ThermaCare HeatWraps produced a rapid and sustained increase in skin temperature (Fig 1). Mean (SD) skin temperature was 30.2°C (0.7°C) at baseline, increasing to 37.4°C (0.7°C) at 30 minutes and 38.0°C (0.8°C) at 2 hours. This increase over baseline of 7.8°C (25.8%) was statistically significant ( $P = .001$ ). The difference in skin temperature change was significant for ThermaCare HeatWraps vs Icy Hot Cream ( $P < .002$ ) and Patch ( $P = .002$ ), as can be easily visualized in the thermal images (Fig 2).

### Muscle Temperature

Both Icy Hot products produced a modest, gradual cooling effect on muscle tissue (Fig 3). After application of Icy Hot Cream, muscle temperature decreased from a mean (SD) of 34.0°C (0.5°C) at baseline to 33.0°C (0.5°C) at 2 hours—a change of -1.0°C (-2.9%;  $P = .01$ ). With Icy Hot Patches, muscle temperature decreased from a mean (SD) of 35.2°C (0.7°C) at baseline to 33.9°C



**Fig 1.** Skin temperature in first 2 hours after application of ThermoCare HeatWraps, Icy Hot Cream, or Icy Hot Patch.

(0.5°C) at 2 hours, a change of  $-1.3^{\circ}\text{C}$  ( $-3.8\%$ ) over the 2-hour evaluation ( $P = .01$ ).

After an initial lag of about 30 minutes, ThermoCare HeatWraps began producing an increase in muscle temperature that continued to rise gradually until the end of the 2-hour assessment (Fig 3). Muscle temperature was a mean (SD) of  $34.8^{\circ}\text{C}$  ( $0.6^{\circ}\text{C}$ ) at baseline,  $34.8^{\circ}\text{C}$  ( $0.7^{\circ}\text{C}$ ) at 15 minutes, rose to  $35.9^{\circ}\text{C}$  ( $0.6^{\circ}\text{C}$ ) at 30 minutes, and reached  $37.5^{\circ}\text{C}$  ( $0.7^{\circ}\text{C}$ ) at 2 hours. Thus, 2 hours after application, ThermoCare HeatWraps increased muscle temperature by a mean of  $2.7^{\circ}\text{C}$  ( $7.7\%$ ;  $P = .002$ ). As with skin temperature findings, the muscle temperature changes observed between ThermoCare HeatWraps and either Icy Hot product were statistically significant ( $P = .007$  vs Cream;  $P = .003$  vs Patch).

**Core Temperature**

Core temperature was unchanged under any of the 3 topical treatment conditions. Mean core temperature at

baseline was  $98.6^{\circ}\text{C}$ ,  $98.7^{\circ}\text{C}$ , and  $98.7^{\circ}\text{C}$  in the Icy Hot Cream, Icy Hot Patch, and ThermoCare HeatWraps groups, respectively. After 2 hours, mean core temperature was  $98.5^{\circ}\text{C}$ ,  $98.7^{\circ}\text{C}$ , and  $98.7^{\circ}\text{C}$  with these treatments, respectively.

**Skin Blood Flow**

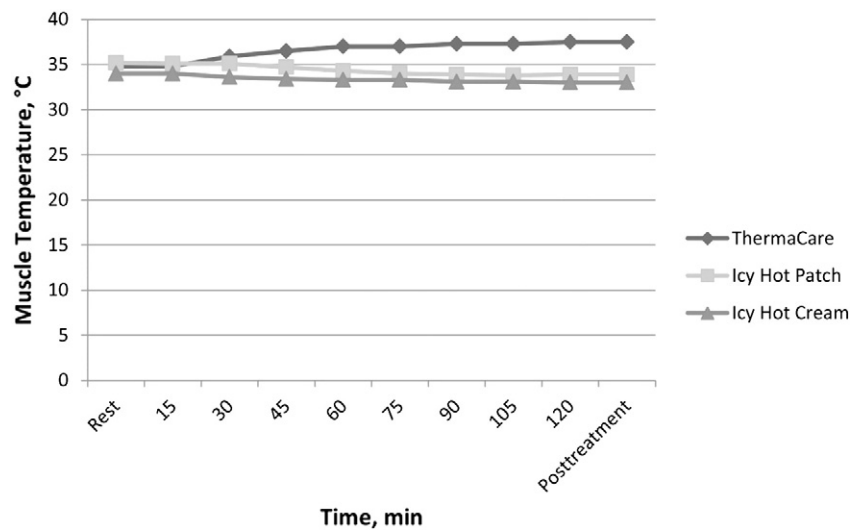
Differences in skin blood flow at baseline were observed in the 3 treatment groups, but these differences were not statistically significant.

The 2 Icy Hot products differed in their effect on skin blood flow (Fig 4). With Icy Hot Cream, skin blood flow initially increased from a mean (SD) of 144.2 (14.3) flux at baseline to a maximum of 156 (16.5) flux at 30 minutes and then steadily declined to 87.5 (13.2) flux at 2 hours. The net change from baseline to 2 hours was  $-56.7$  flux or ( $-39.3\%$ ;  $P = .003$ ).

Icy Hot Patches produced a rapid decrease in mean (SD) blood flow in skin from 114.3 (11.6) flux at baseline



**Fig 2.** Thermal image of skin over the quadriceps muscle 2 hours after application of (A) Icy Hot Cream, (B) Icy Hot Patch, and (C) ThermoCare HeatWraps. Yellow indicates cooler temperature; red and blue indicate hotter temperature. *Dist*, distance from subject in meters;  $\epsilon$ , emissivity; *Trefl*, reflected apparent temperature.



**Fig 3.** Muscle temperature in first 2 hours after application of ThermaCare HeatWraps, Icy Hot Cream, or Icy Hot Patch.

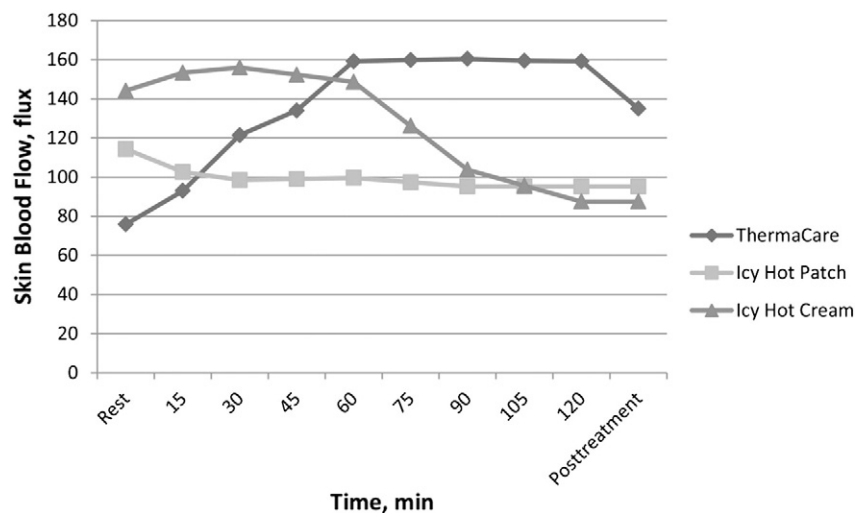
to 102.6 (14.3) flux at 15 minutes and then 98.5 (21.4) flux at 30 minutes, after which it declined more slowly to 95.2 (20.7) flux at 2 hours. Mean change over the 2-hour application period was  $-19.1$  flux ( $-16.7\%$ ;  $P = .045$ ).

With ThermaCare HeatWrap application, blood flow increased steadily during the first hour of application, from a mean (SD) of 75.9 (18.1) flux at baseline to 159.2 (27.3) flux at 60 minutes, after which it remained fairly constant, with a final mean value at 2 hours of 159.2 (35.0) flux. This represented a statistically significant increase in skin blood flow of 83.3 flux or 109.7% ( $P = .0003$ ) from baseline (Fig 4). The effect on skin blood flow at 2 hours was significantly greater for ThermaCare HeatWraps compared with Icy Hot Cream ( $P = .001$ ) or Patch ( $P = .002$ ).

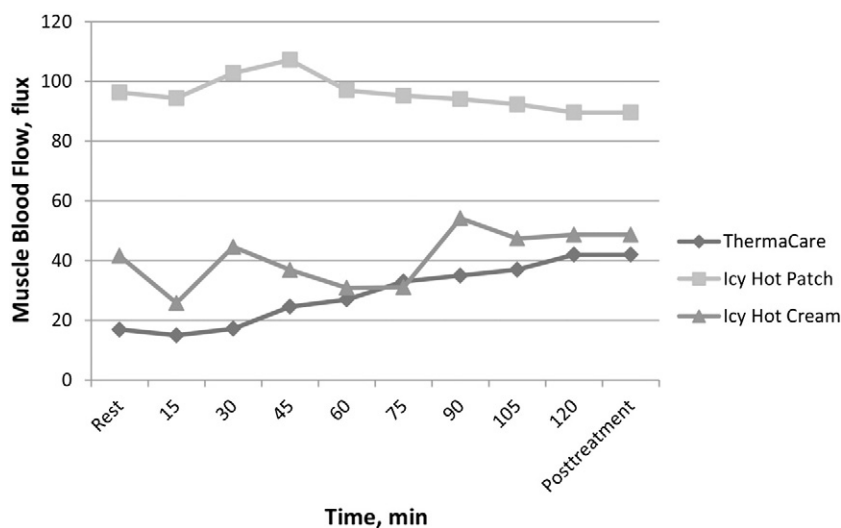
### Muscle Blood Flow

Differences in muscle blood flow were observed at baseline among the 3 treatment arms. These differences may have been attributable to differences in the area sampled by the probe (eg, middle of the muscle vs near the fascia).

Icy Hot Cream produced an erratic effect on blood flow in the quadriceps muscle over the course of the 2-hour assessment period (Fig 5). Muscle blood flow mean (SD) was 41.6 (4.2) flux at baseline, dropped to 25.8 (4.9) flux at 15 minutes, rose to 44.6 (5.1) flux at 30 minutes, and continued to fluctuate for the remainder of the study, reaching 48.7 (6.4) flux at 2 hours. The resulting net increase in mean muscle blood flow from



**Fig 4.** Skin blood flow in first 2 hours after application of ThermaCare HeatWraps, Icy Hot Cream, or Icy Hot Patch.



**Fig 5.** Muscle blood flow in first 2 hours after application of ThermoCare HeatWraps, Icy Hot Cream, or Icy Hot Patch.

baseline to 2 hours was 7.0 flux (16.9%;  $P = .02$ ), although there was a 28.4-flux difference between peak (54.2 flux) and nadir (25.8 flux) of muscle blood flow after Icy Hot Cream application.

Icy Hot Patch produced an initial rise in muscle blood flow followed by a slow, steady decrease to below baseline level (Fig 5). Mean (SD) muscle blood flow was 96.3 (5.8) flux at baseline, peaked at 107.2 (6.4) flux at 45 minutes, and then decreased to a low of 89.6 (3.7) flux at 2 hours. Net change from baseline to 2 hours was  $-6.7$  flux or ( $-7.0\%$ ;  $P = .02$ ).

After an initial lag of about 30 minutes, ThermoCare HeatWraps produced a steady increase in muscle blood flow, increasing it nearly 1.5-fold (Fig 5). Mean (SD) blood flow in the quadriceps was 16.9 (4.2) flux at baseline and rose to 42.0 (6.3) flux after 2 hours of ThermoCare HeatWrap application, a net increase of 25.1 flux (148.5%;  $P = .004$ ).

## Discussion

The present investigation was a longitudinal study of the effect of heat and menthol on tissue temperature and blood flow. As such, each subject was their own control and the pretest to posttest difference required no control group. To our knowledge, this is the first study directly comparing the effects of heat wraps vs menthol-containing topical analgesics on skin and muscle temperature and blood flow.

As expected, application of ThermoCare HeatWrap quickly warmed the skin by 25.8% and caused a corresponding 7.7% rise in the temperature of the

underlying muscle tissue, as would be predicted from the Pennes heat transfer equations.<sup>31</sup> There were a concurrent 109.7% increase in skin blood flow and 148.5% increase in muscle blood flow with ThermoCare HeatWrap use. These results are consistent with those of other studies, which have shown that heat, even at low levels, results in vasodilation and increased blood flow.<sup>32,33</sup> The vasodilation results from 2 different mechanisms. Initially, heat prompts rapid vasodilation by promoting release of neurotransmitters (eg, calcitonin gene-related peptide and substance P) from endothelial cells.<sup>32,34</sup> A second, independent, more gradual increase in blood flow resulting from heat may be mediated by activation of endothelial nitric oxide (NO) synthase and production of NO to produce vasodilation.<sup>34,35</sup> In deep tissues such as muscle, heat may have a direct effect on blood flow and increases in tissue metabolism. Edwards et al<sup>36</sup> observed  $Q_{10}$  values averaging 3.4 in quadriceps muscle. In other words, for each 10°C increase in temperature, tissue metabolism increases by a factor of 3.4. Increased blood flow has been shown to promote tissue healing by increasing oxygen delivery, removing metabolites, and enhancing metabolism in damaged muscle tissue.<sup>21</sup>

Analgesic and vascular effects of heat are, at least in part, mediated through activation of TRP membrane channels. There are 28 different mammalian TRP membrane channels,<sup>37</sup> which can be activated by temperature, pain, tissue osmolarity, oxidative stress, lipids, intracellular calcium elevation, cooling agents (eg, menthol, icilin), and other factors.<sup>38</sup> Seven of these channels are responsive to warmth or heat (TRPV1, TRPV2, TRPV3, TRPV4, TRPM2, TRPM4, and TRPM5), and 2 detect cool or cold temperatures (TRPA1 and TRPM8).<sup>37</sup>

TRPV1 receptors play a role in nociceptive pain processing.<sup>37,39,40</sup> Intense exercise provokes an increase in intravascular adenosine triphosphate (ATP), which plays a role in regulating skeletal muscle blood flow.<sup>41,42</sup> In addition, ATP activates various P2X receptors involved in pain perception, particularly P2X<sub>3</sub>.<sup>39,43</sup> Activation of TRPV1 inhibits P2X<sub>3</sub> signaling, probably through cross talk between these colocalized receptors.<sup>39</sup> Another plausible mechanism is that activation of TRPV1 receptors, which can occur with heat, menthol, capsaicin, or ATP, causes an influx of Ca<sup>++</sup> into skin sensory nerves, inactivating P2X receptors and producing TRPV1 desensitization.<sup>21,39,40,44,45</sup>

Our findings of increased temperature and blood flow suggest that ThermaCare HeatWraps have the potential to provide both analgesia and improved tissue healing. This is consistent with results from one of our previous studies in which application of low-level heat wraps following exercise enhanced muscle healing as evidenced by reductions in fascial edema (measured on ultrasonography), white cell counts, and heat shock protein 27 (a biomarker for muscle damage).<sup>21</sup> Similarly, Hassan<sup>46</sup> reported that young men given a 30-minute warm water bath (38°C) 15 minutes after exercise experienced less of an increase in serum skeletal muscle troponin I, creatine kinase, and myoglobin (biomarkers of muscle damage) at 2 and 6 hours postexercise compared with those who underwent either no thermal application or cold water exposure (20°C for 30 minutes).

In contrast to our findings with ThermaCare HeatWraps, the 2 menthol-containing products (Icy Hot Patches and Cream) brought about a modest cooling effect in skin and muscle tissue. The Icy Hot Patch caused a reduction in blood flow in both skin (~17%) and muscle (7%). After 2 hours, Icy Hot Cream had a net effect of reducing skin blood flow 39%, whereas blood flow to muscle increased by 17% above baseline levels. We attribute the difference in the effect of Icy Hot Cream on blood flow in skin vs muscle to the fact that alcohol evaporation on skin may lead to a cooling effect, whereas the menthol penetrates to muscle, where it may have a direct effect on blood flow. Our findings with regard to menthol counter the hypothesis that menthol's effects on TRP receptors might block the response to cold, thereby altering the receptor cold/warmth balance in favor of tissue warming.<sup>47</sup> Rather, it seems likely that menthol's stimulation of TRPM8 receptors reduces peripheral pain and provides a general feeling of cooling resulting from reduction in blood flow.<sup>48,49</sup> Evaporative heat loss may also be a contributing factor. Thus, the analgesia provided by menthol-containing products is less likely to be accompanied by tissue healing compared with the

use of nonmenthol heat products. This should be taken into consideration, along with the potential for chemical burns associated with menthol-containing products,<sup>50</sup> when recommending OTC therapies to patients with DOMS or other forms of muscle soreness.

It is noteworthy that skin and muscle cooling was seen even with the Icy Hot Cream, which also contains methyl salicylate. Aspirin directly stimulates endothelial NO synthase to form NO,<sup>51</sup> which in turn induces vasodilation, increasing blood flow.<sup>34,35</sup> However, it appears from our results that the nonsteroidal anti-inflammatory drug effect of vasodilation was counteracted by the effects of menthol because blood flow was reduced rather than increased. It is also noteworthy that, for both skin and muscle, the blood flow–temperature ratio showed the greatest deviations over time with the Icy Hot Cream. This suggests that blood flow's sensitivity to temperature was affected by some factor other than temperature—most likely methyl salicylate, which is present in the Icy Hot Cream but not the other products.

Menthol is a topical analgesic of the counterirritant class.<sup>52</sup> A previous study showed that, as shown here, menthol caused a small decrease in skin temperature,<sup>53</sup> but skin temperature reduction did not differ significantly with menthol concentration (ie, 0.5%, 4.6%, and 10.0%). Unfortunately, this study did not examine blood flow and muscle temperature.<sup>53</sup> In another study, skin blood flow measurements after application of menthol did not differ significantly from baseline values.<sup>54</sup> In the present study, Icy Hot Patch reduced local blood flow, and Icy Hot Cream had contradictory effects on skin and muscle blood flow. These findings suggest that, whereas all of these products may have an analgesic effect, heat wraps are likely the superior choice to facilitate repair of damaged muscle tissue in DOMS and similar conditions.

## Limitations

Limitations of our study include its small sample size and nonrandomized open-label design. However, all participants received all 3 treatments, and objective measures were used to assess temperature and blood flow, limiting their subjectiveness to bias. This study was conducted in a population of pain-free individuals, so it was not possible to compare analgesic effects or evaluate any correlation between analgesia and either temperature or blood flow. Assessments were limited to the first 2 hours after product application; however, ThermaCare HeatWraps and Icy Hot Patches are recommended for up to 8 hours of use.<sup>22,26,27</sup> Further study is needed to determine effects on skin and muscle



temperature and blood flow through 8 hours of treatment and following product removal. Replication in a larger population of patients with DOMS would be informative, as would assessment of biomarkers of muscle damage during and after treatment.

## Conclusion

In this study of 15 healthy adults, ThermoCare HeatWraps increased skin and intramuscular temperature, and local blood flow. In contrast, topical analgesics containing menthol with or without a prostaglandin inhibitor had a cooling effect on skin and muscle temperature.

## Funding Sources and Conflicts of Interest

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