

# Over-the-counter Topical Musculoskeletal Pain Relievers Used With a Heat Source: A Dangerous Combination



Shayna C. Rivard, MD; Megan A. Brelsford, DO; Neil F. Gibbs, MD

## PRACTICE POINTS

- Recognize the potential complication of burn from use of over-the-counter (OTC) musculoskeletal relievers in combination with a heat source.
- Screen for OTC product use as well as device application when evaluating an atypically patterned cutaneous eruption.
- Recognize potential toxicity associated with both topical application and accidental ingestion in the pediatric population.
- Physicians should become familiar with resources available, including patient handouts that describe risks associated with use of OTC musculoskeletal relievers containing methyl salicylate and menthol ingredients.

To the Editor:

The combination of menthol and methyl salicylate found in a variety of over-the-counter (OTC) creams in conjunction with a heat source such as a heating pad used for musculoskeletal symptoms can be a dire combination due to increased systemic absorption with associated toxicity and localized effects ranging from contact dermatitis or irritation to burn or necrosis.<sup>1-6</sup> We present a case of localized burn due a combination of topical methyl salicylate and heating pad use. We also discuss 2 commonly

encountered side effects in the literature—localized burns and systemic toxicity associated with percutaneous absorption—and provide specific considerations related to the geriatric and pediatric populations.

A 62-year-old woman with a history of eczematous dermatitis and osteoarthritis with pain of the left shoulder presented to the dermatology clinic with painful skin-related changes on the left arm of 1 week's duration. She was prescribed acetaminophen and ibuprofen. However, she self-medicated the left shoulder pain with 2 OTC products containing topical menthol and/or methyl salicylate in combination with a heating pad and likely fell asleep with this combination therapy applied. She noticed the burn the next morning. On examination, the left arm exhibited a geometric, irregularly shaped, erythematous, scaly plaque with a sharp transverse linear demarcation proximally and numerous erythematous linear scaly plaques oriented in an axial orientation with less-defined borders distally (Figure). The patient was diagnosed with burn secondary to combination of topical methyl salicylate and heating pad use. The patient was advised to discontinue the topical medication and to use caution with the heating pad in the future. She was prescribed pramoxine-hydrocortisone lotion to be applied to the affected area twice daily up to 5 days weekly until resolution. Subsequent evaluations revealed progressive improvement with only mild postinflammatory hyperpigmentation noted at 6 months after the burn.

Dr. Rivard is from the Division of Dermatology, US Naval Hospital Guam, Tutuhan. Dr. Brelsford was from and Dr. Gibbs is from the Department of Dermatology, Naval Medical Center, San Diego, California. Dr. Brelsford currently is from Naval Medical Center Portsmouth, Virginia.

The authors report no conflict of interest.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the US Government.

Correspondence: Shayna C. Rivard, MD, Division of Dermatology, US Naval Hospital Guam, Bldg #50, Farenholt Ave, Tutuhan, Guam 96910.



A geometric plaque on the left arm at the site of combined methyl salicylate and heating pad use.

The US Food and Drug Administration (FDA) released statements in 2012 regarding concern for burns related to use of OTC musculoskeletal pain relievers, with 43 cases of burns reported due to methyl salicylate and menthol from 2004 to 2010. Most of the second- and third-degree burns occurred following topical applications of products containing either menthol monotherapy or a combination of methyl salicylate and menthol.<sup>1,2</sup> In 2006, the FDA had already ordered 5 firms to stop compounding topical pain relief formulations containing these ingredients, with concerns that it puts patients at increased risk because the compounded formulations had not received FDA approval.<sup>3</sup> Despite package warnings, patients may not be aware of the concerning side effects and risks associated with use of OTC creams, especially in combination with occlusion or heating pad use. Our case highlights the importance of ongoing patient education and physician counseling when encountering patients with arthritis or musculoskeletal pain who may often try various OTC self-treatments for pain relief.<sup>7</sup>

In 2012, the FDA reports stated that the cases of mild to serious burns were associated with methyl salicylate and menthol usage, in some cases 24 hours after first usage. Typically, these effects occur when concentrations are more than either 3% menthol alone or a combination of more than 3% menthol and more than 10% methyl salicylate.<sup>1,2</sup> In our case, the patient had been using 2 different OTC products that may have contained as much as 11% menthol and/or 30% methyl salicylate. Electronic resources are available that disclose safety instructions including not to occlude the site, not to use on wounds, and not to be used in conjunction with a

heating pad.<sup>8,9</sup> Skin breakdown and vasodilation are more likely to occur in a setting of heat and occlusion, which allows for more absorption and localized side effects.<sup>4,10</sup> Localized reactions may range from contact dermatitis<sup>4</sup> to muscle necrosis.<sup>5</sup>

The most noteworthy case of localized destruction described a 62-year-old man who had applied topical methyl salicylate and menthol to the forearms, calves, and thighs, then intermittently used a heating pad for 15 to 20 minutes (total duration).<sup>5</sup> He subsequently developed erythema and numerous 7.62- to 10.16-cm bullae, which was thought to be consistent with contact dermatitis. Three days later, he was found to have full-thickness cutaneous, fascial, and muscle necrosis in a linear pattern. He was hospitalized for approximately 1 year and treated with extensive debridement and a skin graft. His serum creatinine level increased from 0.7 mg per 100 mL to 2.7 mg per 100 mL (reference range, 0.6–1.2 mg/dL) with evidence of toxic nephrosis and persistent interstitial nephritis, demonstrating the severity of localized destruction that may result when combining these products with direct heat and potential subsequent systemic consequences of this combination.<sup>5</sup>

The systemic absorption of OTC formulations also has been studied. Morra et al<sup>10</sup> studied 12 volunteers (6 women, 6 men) who applied either 5 g of methyl salicylate ointment 12.5% twice daily for 4 days to an area on the thigh (approximately equal to 567 mg salicylate) or trolamine cream 10% twice for 1 day. The participants underwent a break for 7 days and then switched to the alternate treatment. They found that 0.31 to 0.91 mg/L methyl salicylate was detected in the serum 1 hour after applying the ointment consisting of methyl salicylate, and 2 to 6 mg/L methyl salicylate was detected on day 4. Therapeutic serum salicylate levels are 150 to 300 mg/L. They found that approximately 22% of the methyl salicylate also was found in urine samples on day 4. Although these figures may appear small, this study was prompted when a 62-year-old man presented to the emergency department with symptoms of salicylate toxicity and a serum concentration of 518 mg/L from twice-daily use of an OTC formulation containing methyl salicylate over the course of multiple weeks.<sup>10</sup> Additionally, those who have aspirin hypersensitivity should be cautious when using such products due to the risk for reported angioedema.<sup>4</sup>

Providers must exercise extreme caution while caring for geriatric patients, especially if patients are taking warfarin. The combined effects of warfarin and methyl salicylate have previously caused cutaneous purpura, gastrointestinal bleeding, and elevated international normalized ratio values.<sup>4,10</sup> Older individuals also have increased skin fragility, allowing microtraumatic insult to easily develop. This fragility, along with an overall decreased intactness of the skin barrier, may lead to increased skin absorption. Furthermore, the addition of applying any heat source places the geriatric patient at greater risk for adverse events.<sup>10</sup>

In considering the limits of age, the pediatric population also has been studied regarding salicylate toxicity. Most commonly, oral ingestion has caused fatalities, as oil of wintergreen has been cited as extremely dangerous for children if swallowed; doses as small as a teaspoon (5 mL: 7000 mg salicylate) have resulted in fatalities.<sup>4,6</sup> Although the consumption of a large amount of a cream- or ointment-based product is unlikely due to the consistency of the medication,<sup>6</sup> the thought does merit consideration in the inquisitive toddler age group. For a 15-kg toddler, 150 mg/kg of aspirin or 2250 mg of aspirin, is considered the toxic level, which upon conversion to methyl salicylate levels using a 1.4 factor equates to 1607 mg of methyl salicylate to reach toxicity.<sup>6</sup> If using a product with methyl salicylate 30% composition, 1 g of the product contains 300 mg of methyl salicylate; therefore if the toddler consumed approximately 5.3 g of the product (1607 mg methyl salicylate [toxic level] divided by 300 mg methyl salicylate per 1 g of product), he/she would reach toxic levels.<sup>6,11</sup> To put this into perspective, a 2-oz tube contains 57 g (approximately 10 times the toxic dose) of the product.<sup>8</sup> Thus, although there is less concern overall for consumption of cream- or ointment-based methyl salicylate, there still is potential for harm if a small child were to ingest such a product containing higher percentages of methyl salicylate.<sup>6</sup>

There also have been reports of pediatric toxicity related to percutaneous absorption, even leading to pediatric fatality.<sup>4,6</sup> In particular, there was a case of a young boy hospitalized with ichthyosis who received escalating doses of percutaneous salicylate, which resulted in toxicity; when therapy was discontinued, he experienced full recovery.<sup>12</sup> In 2007, a 17-year-old adolescent girl died from methyl salicylate toxicity after numerous applications of salicylate-containing products in conjunction with medicated pads.<sup>7</sup>

Although the FDA has drawn attention and encouraged caution with use of OTC topical musculoskeletal pain relievers, the importance of ensuring patients are fully aware of potential burns, permanent skin or muscle damage, and even death if used inappropriately cannot

be overstated. The FDA consumer health information website has 2 patient-directed handouts<sup>2,3</sup> that may be useful to post in patient waiting areas to increase overall understanding of the risks associated with OTC products containing methyl salicylate and menthol ingredients. Fortunately, our patient suffered only mild postinflammatory hyperpigmentation without substantial sustained consequences.

## REFERENCES

1. US Food and Drug Administration. FDA Drug Safety Communication: rare cases of serious burns with the use of over-the-counter topical muscle and joint pain relievers. <http://www.fda.gov/Drugs/DrugSafety/ucm318858.htm>. Published September 13, 2012. Updated February 11, 2016. Accessed October 31, 2017.
2. US Food and Drug Administration. Topical pain relievers may cause burns. <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm318674.htm>. Published September 13, 2012. Updated November 5, 2015. Accessed October 31, 2017.
3. US Food and Drug Administration. Use caution with over-the-counter creams, ointments. <http://www.fda.gov/forconsumers/consumerupdates/ucm049367.htm>. Updated October 17, 2017. Accessed October 31, 2017.
4. Chan TY. Potential dangers from topical preparations containing methyl salicylate. *Hum Exp Toxicol*. 1996;15:747-750.
5. Heng MC. Local necrosis and interstitial nephritis due to topical methyl salicylate and menthol. *Cutis*. 1987;39:442-444.
6. Davis JE. Are one or two dangerous? methyl salicylate exposure in toddlers. *J Emerg Med*. 2007;32:63-69.
7. Associated Press. Sports cream warnings urged after teen's death: track star's overdose points to risks of popular muscle salve. *NBC News*. <http://www.nbcnews.com/id/19208195>. Updated June 13, 2007. Accessed October 31, 2017.
8. Ultra Strength Bengay Cream. Bengay website. <http://www.bengay.com/bengay-ultra-strength-cream>. Accessed November 1, 2017.
9. Tiger Balm Arthritis Rub. Tiger Balm website. [http://www.tigerbalm.com/us/pages/tb\\_product?product\\_id=6](http://www.tigerbalm.com/us/pages/tb_product?product_id=6). Accessed November 1, 2017.
10. Morra P, Bartle WR, Walker SE, et al. Serum concentrations of salicylic acid following topically applied salicylate derivatives. *Ann Pharmacother*. 1996;9:935-940.
11. US National Library of Medicine. Bengay Ultra Strength non greasy pain relieving- camphor (synthetic), menthol, and methyl salicylate cream. Daily Med website. <http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=5aa265f8-ab45-47b2-b5ab-d4df54daed01>. Updated November 3, 2016. Accessed November 1, 2017.
12. Aspinall JB, Goel KM. Salicylate poisoning in dermatological therapy. *Br Med J*. 1978;2:1373.