Topical analgesics as alternative first-line agents

Supported by an educational grant from Hisamitsu America, Inc
This activity is provided by Global Education Group
Accreditation
This activity is available for credit from 1/01/2021 to 12/31/2021.

Target audience
Healthcare providers who treat and manage acute and chronic pain, including Internists, Health System Pharmacists, Nurse Practitioners, Primary Care Physicians, Physician Assistants, Physical Therapists, and Psychologists.

Statement of need/program overview
As the opioid crises continues to loom over the landscape of pain management, there is a growing interest among practitioners for alternative analgesia and delivery systems. As such, topical and transdermal therapeutic options are being utilized with greater frequency among pain practitioners.

Jeff Gudin MD
Clinical Associate Professor, Department of Anesthesiology and Perioperative Medicine
Rutgers NJ Medical School, Department of Anesthesiology and Pain Management
University of Miami School of Medicine
Dr. Gudin is Board Certified in Pain Medicine, Anesthesiology, Addiction Medicine, Palliative Care.

Disclosures
Stock Shareholder: Analgesic Strategies, Virpax Pharmaceuticals

Learning objectives
• Discuss adverse effects associated with systemic analgesics
• Identify anatomic targets for topical medications
• Identify active ingredients well suited for topical delivery
• Differentiate formulations of topically applied medication
• Explain the effectiveness and potential adverse reactions of topical preparations

Physician accreditation statement
Global Education Group is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Physician credit designation
Global Education Group designates this continuing education activity for 0.5 contact hour(s) (0.05 CEUs) of the Accreditation Council for Pharmacy Education. UAN: 0530-0000-20-326-H8-P

This is a knowledge based activity.

Global contact information
For information about the accreditation of this program, please contact Global at: (303) 395-2782 or cme@globaleducationgroup.com.

Instructions to receive credit
In order to claim credit, please go to https://pain.sh/xuz to complete the online posttest and evaluation. You must earn a score of at least 70% in order to be awarded CME.

Fee information & refund/cancellation policy
There is no fee for this educational activity.

Disclosure of conflicts of interest
Global Education Group (Global) requires instructors, planners, managers and other individuals and their spouse/life partner who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by Global for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis for content, and appropriateness of patient care recommendations.

The planners and managers reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

<table>
<thead>
<tr>
<th>Name of planner or manager</th>
<th>Reported financial relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashley Marostica, RN, MSN</td>
<td>Nothing to disclose</td>
</tr>
<tr>
<td>Lindsay Borvansky</td>
<td>Nothing to disclose</td>
</tr>
<tr>
<td>Andrea Funk</td>
<td>Nothing to disclose</td>
</tr>
<tr>
<td>Liddy Knight</td>
<td>Nothing to disclose</td>
</tr>
</tbody>
</table>

Disclosure of unlabeled use
This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. Global Education Group (Global) does not recommend the use of any agent outside of the labeled indications.

The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of any organization associated with this activity. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

Disclaimer
Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed in this activity should not be used by clinicians without evaluation of patient conditions and possible contraindications on dangers in use, review of any applicable manufacturer’s product information, and comparison with recommendations of other authorities.
Abstract

Topical analgesics are gaining in popularity with support from published data and medical society guidelines. The benefits seem clear: limited systemic absorption minimizing the potential for adverse events. Clinicians need to be aware of the classes of analgesics available for delivery through the skin, as well as their advantages and potential side effects. In addition to prescription products, data are emerging about effectiveness of over-the-counter (OTC) preparations. With the refractory nature of many chronic pain syndromes, the addition of topical analgesics may allow patients to avoid oral NSAIDs, opioids, and other systemic agents associated with adverse effects.

Systemic analgesics

The main purpose of systemic analgesics is to target various receptors in the peripheral and central nervous system (CNS). By nature, their administration delivers medications nonselectively to end organs and, therefore, brings about unwanted adverse effects. Some of the more common types of systemic agents are mu opioid analgesics, acetaminophen, and NSAIDs; adjuvants include anticonvulsants, antidepressants, muscle relaxants, and steroids.

A myriad of adverse events are associated with systemic agents, ranging from bothersome issues such as sweating, itching, and constipation to potentially dangerous consequences including respiratory depression, overdose, death, and end organ problems such as hepatic, renal, cardiovascular, and gastrointestinal dysfunction.

Topically administered medications

Benefits

A number of purported benefits are associated with topically administered medications. One is avoidance of issues related to gastrointestinal problems for patients with swallowing difficulties, or persistent nausea or vomiting, because there is no need to absorb these medicines from the gastrointestinal tract. Hepatic first-pass effect is eliminated because these medications are parenteral, not orally administered. With systemic agents, higher plasma concentrations are desired. With topical agents, higher tissue concentrations are the goal. Minimizing high plasma concentrations more than likely minimizes the associated adverse effects. Literature supports that topical analgesic use allows patients to lower their consumption of oral analgesics, and there is a simplicity and convenience to the administration of these topicals that has the potential to increase compliance and/or quality of life. Clearly, the targets for topically-applied medications are musculoskeletal or neurological structures in the periphery. The goal is to bind, activate, or inhibit certain receptors under the skin, deep musculoskeletal tissues, and/or joints without significant absorption throughout the rest of the body.

The American Academy of Orthopedics and the American College of Rheumatology support the use of topical NSAIDs to manage conditions such as osteoarthritis. Internationally, European leagues like Osteoarthritis Research Society International and Asian societies such as the Chinese Medicine Expert Consensus and Singapore Ministry of Health have all supported the use of topical analgesics as first-line therapies. More recently, the American College of Physicians and the American Academy of Family Practice released a clinical guideline on the Nonpharmacologic and Pharmacologic Management of Acute Pain From Non–Low Back, Musculoskeletal Injuries in Adults. This guideline recommends using topical NSAIDs with or without menthol gel as first-line therapy to reduce or relieve symptoms (including pain), improve physical function, and improve
Topical analgesics as alternative first-line agents

treatment satisfaction (a strong recommendation based on moderate-certainty evidence).7

Ingredients
NSAIDs are the most common ingredient of topical preparations. Local anesthetics are a close second, with the lidocaine patch in various formulations available both by prescription and OTC. Rubefacients, such as camphor, menthol, and wintergreen oil (known as methyl salicylate), produce a counterirritant or warming/heating effect. Capsaicin activates a thermal sensitive family of receptors. Opioids can also be applied topically. Clonidine, which comes in a topical patch preparation, is often compounded into creams and gels. Ketamine and cannabinoids are also commonly included in topical preparations.

Topical local anesthetics

Local anesthetics relieve pain by reducing ectopic discharges of somatic nerves in areas of localized pain and suppressing abnormal painful spontaneous discharges. Topical local anesthetics are available in a number of formulations: patches (called “plasters” in other parts of the world), sprays, creams, and gels. An EMLA—eutectic mixture of local anesthetics—is a cream that contains 2.5% prilocaine and 2.5% lidocaine, and has a fairly rapid onset. EMLA is used in pediatrics to blunt the response to painful needle sticks and procedures.

Lidocaine
The lidocaine patch has been in use >20 years; lidocaine jelly or creams have been in use even longer. In the United States, the lidocaine patch 5% is approved for use in patients with postherpetic neuralgia. Newer patch formulations are available with significantly lower amounts of the drug: the original patch contains 700 mg lidocaine while newer bioequivalent patches contain 36 mg but deliver the same amount of lidocaine through the skin. Even with up to 3 patches applied for 12 hours, systemic levels reach approximately 1/20 that of toxicity range.8

There is a newer prescription lidocaine patch system approved that is 1.8%, containing almost 20 times less lidocaine than the original patch, suggesting that formulation really makes a difference.9 Lidocaine patches are also widely available OTC at strengths up to 4%. The pharmacokinetics for these products is mostly unknown, and may indeed be similar to some prescription strength products as both formulation (penetration) and adhesion of the patch system affect drug delivery.

Lidocaine is relatively safe. When administered topically, however, if too much is applied, the risk of toxicity increases, although using up to 3 patches and applying as directed is typically not associated with systemic adverse events. The most common adverse events are skin reactions, which often has more to do with the adhesive than with the drug. Compared to IV administration, the plasma concentrations are about 20 times or more lower than that seen with systemic administration.8

OTC lidocaine patch study
A study compared OTC patches containing both lidocaine and menthol to prescription 5% lidocaine patches and placebo in patients with back pain and arthritic pain syndromes.10 The double-blind, placebo-controlled study compared 3 groups of a total of 87 patients and looked for superiority to placebo and noninferiority to Lidoderm®. The OTC patch was noninferior to the 5% lidocaine patch. When compared to placebo for efficacy, general activity, and normal work, OTC proved superior with similar side effect profiles. Research theorized that menthol’s ability to increase skin permeability—a local vasodilating effect—facilitated more efficient drug delivery to the site of pain, causing higher than expected efficacy.10 While it might have been the menthol, it also might have been
the quality of the patch technology. A recently published paper discussed the importance of formulation in the patch.\textsuperscript{11} If some OTC patches are as efficacious as prescription patches, there may be benefits simply because OTCs typically tend to be lower cost products.

**Topical NSAIDs**

NSAIDs are widely utilized as an ingredient in topical analgesics around the world. They produce high concentration in the dermis, synovium, muscle tissue, and joint cartilage, yet their bioavailability is low, ranging from 5% to 15% of that observed after systemic administration. Formulations that facilitate tissue penetration may improve efficiency in deeper sites, such as joints.\textsuperscript{12} There are varying reports about efficacy of topical NSAIDs for musculoskeletal pain. A Cochrane Review of NSAIDs in the United States and around the world looked at >10,000 patients mostly with osteoarthritis of the knee.\textsuperscript{13} The primary outcome measure was the clinical success rate of ≥50% reduction in pain intensity. Although many agents were studied, there were only enough data for diclofenac and ketoprofen to do a pooled analysis. The diclofenac number needed to treat was 9.8, and for topical ketoprofen, 6.9. Researchers concluded that the use of topical NSAIDs such as diclofenac and ketoprofen provide good levels of pain relief in knee osteoarthritis in people >40 years of age.\textsuperscript{13}

A collaborative effort by the American College of Physicians and the American Academy of Family Physicians looked at pharmacologic and nonpharmacologic management of acute pain from non-low back musculoskeletal injuries in adults.\textsuperscript{7} Researchers evaluated the following clinical outcomes using the GRADE system (Grading of Recommendations Assessment, Development and Evaluation) for levels of evidence: pain at ≤2 hours and 1 to 7 days), physical function, symptom relief, treatment satisfaction, and adverse events. The conclusion: for clinicians who treat patients with acute pain from non-low back musculoskeletal injuries, topical NSAIDs, with or without menthol gel, should be used as a first-line therapy. This was a strong recommendation with moderate certainty evidence. The guideline also suggested using oral NSAIDs or acetaminophen, acupressure, or transcutaneous electrical nerve stimulation to reduce pain. Importantly, they suggested not using opioids, including tramadol.

**Rubefacients**

Topical rubefacients work by counterirritation. They cause local irritation, local vasodilation, and increased blood flow which contributes to a warming sensation many people find appealing. Perhaps vasodilation helps other agents that are mixed in the compound to bind, penetrate, or work more effectively. A Cochrane Review that assessed topical rubefacients concluded that, although they are relatively safe and well tolerated, more data are needed.\textsuperscript{14} The FDA approved an OTC analgesic patch based largely on the results of a study of a new drug application.\textsuperscript{15} A double-blind, parallel-group, placebo-controlled, multicenter study to determine the efficacy and safety profile of a patch containing 10% methyl salicylate and 3% l-menthol compared it with a placebo patch. The 208 patients were randomly assigned to receive either an active patch or a placebo applied to the affected area of the shoulder, upper back, upper arm, neck, calf, thigh, forearm, or abdomen. Pain intensity was assessed while patients were at rest and with movement for 12 hours after patch application. The primary efficacy end point was the summed pain intensity difference score through 8 hours (SPID\textsubscript{8}) with movement. Safety data, including adverse events, and secondary efficacy end points were also evaluated. Patients receiving the active patch experienced significantly greater pain relief, upwards of 40%, than those patients who wore the placebo patch (mean [standard deviation], 182.6 [131.2] vs 130.1 [144.1]; \(P=0.005\)). Of
interest, the adverse effects were comparable between the study groups, with 7 events seen in the active patch group (6.7%) and 6 events in the placebo patch group (5.8%) with no serious adverse events reported during the study. The conclusion: a single 8-hour application of the methyl salicylate and menthol-specific combination patch provided significant relief of pain associated with mild to moderate muscle strain in adult patients compared to placebo. This is currently the only FDA-approved patch that has indication for up to moderate pain.

A study published recently evaluated a topical analgesic pain relieving patch in reducing pain severity scores and improving function in patients with mild to moderate arthritic, neurological, or musculoskeletal pain. The study examined different types of pain such as arthritic, neurological, or musculoskeletal pain. A treatment group of more than 150 patients were given patches for 14 days, and a control group received no patches. After day 14, a majority of the control group patients crossed over to receive the patch. Patients completed Brief Pain Inventory surveys at baseline and at the end of 14 days of treatment, and were asked “How has your use of pain pills or oral medications changed? What kind of side effects have you had, and how satisfied were you with the treatment?” By day 14, pain severity scores and pain interference scores decreased 49% and 58.1%, respectively. Pain severity and interference scores decreased less in the control group, 12.3% and 14.8%, respectively. In the treatment group, 60.5% used concomitant oral pain medications “a lot less” and 90.8% were very/extremely satisfied with the patch.

This observational analysis examined the benefits of these patches in a small treatment group; further large scale randomized controlled trials should be considered. Nonetheless, the results support the use of this analgesic pain relieving patch as a first-line treatment and should be considered for future pain management guidelines as part of multimodal pain treatment regimens.

**Topical capsaicin**

Capsaicin is a highly selective agonist for the transient receptor potential channel vanilloid-receptor type 1 (TRPV1), which is expressed on central and peripheral terminals of primary sensory neurons. Topical application of capsaicin at the peripheral terminal of TRPV1-expressing neurons superficially denervates the epidermis in humans in a highly selective manner and results in hypoalgesia. Typically, there is significant pain, burning, itching, and/or redness from cutaneous vasodilatation upon initial application due to excitation and sensitization of cutaneous nociceptors; this early reaction then leads to the persistent desensitization and pain relief described above. Capsaicin of various purities and grades has been widely available in pharmacies as low to moderate concentration creams and gels. Knockout studies have revealed the importance of TRPV1 as a molecular pain modulator and target for novel analgesic agents. With animal data and mice bred to not have (“knockout”) TRPV1 receptors, mice respond to pain quite differently, signaling that this is an important molecular target for analgesics.

Capsaicin applied topically denervates (temporarily destroys) peripheral neurons in the cutaneous tissues in a highly selective manner leading to pain relief. Capsaicin is available OTC, can be compounded by pharmacists, and is also available by prescription in higher strengths. In a study of topical capsaicin treatment, epidermal nerve fiber density assessment of the capsaicin treatment group showed that the number of sensory nerve fibers was significantly decreased compared to the placebo/control group. That is the effect of capsaicin, especially in a high dose: it denervates peripheral terminals temporarily yielding pain relief.

An 8% capsaicin patch received approval for the treatment of postherpetic neuralgia in the US in 2009. In Europe this patch is approved for treatment of peripheral neuropathic pain in adults. In patients with painful diabetic
peripheral neuropathy, a single 30-minute application of the capsaicin 8% patch significantly improved pain relief and sleep quality compared with placebo in a 12-week double-blind trial. In 2020, this and other studies led the US FDA to expand the indications for this patch to include the treatment of neuropathic pain associated with diabetic peripheral neuropathy of the feet.20

Topical opioids, palliative care, and wounds

Opioid receptors have been found on peripheral nerves and inflamed tissue.21 Peripheral opioid injections for local analgesia, such as intrarticular morphine, have been found to be effective in several trials.22 Morphine has been used in the palliative care wound treatment setting, and its metabolites are largely undetectable systemically when applied topically to skin ulcers, suggesting the analgesic effect is local. Of note, animal studies indicate that opioids can accelerate wound healing by upregulating nitric oxide synthase.23 The relevance of this for humans is unknown and there is no consensus regarding whether topical opioids benefit or impede wound healing in humans.

Use of relatively insoluble drugs such as morphine, hydromorphone, oxycodone, and hydrophilic drugs were discussed in an article about taking advantage of the peripheral opioid receptor.24 (Fentanyl, which is a lipidsoluble, lipophilic drug that penetrates the skin but is absorbed systemically, was not included.) Although not officially classified as an opioid, carisoprodol produces considerable analgesia when topically applied. The article author disapproved of applying the prodrugs hydrocodone, codeine, or tramadol, which require breakdown to active metabolites.24

Other agents

Other topically applied analgesics, or potential topical analgesics include clonidine, tricyclic antidepressants, baclofen, ketamine, cannabinoinds, gabapentinoids, dextromethorphan, and other local anesthetics and NSAIDs. These agents may see a resurgence in use, especially now that not only US but international guidelines recommend topical analgesics as first-line agents. Why not use a medicine that has little systemic absorption typically, yet could provide a maximum analgesic benefit?

Other common prescription topical pain agents25

- Amantadine 5% – 20%
- Amitriptyline 2% – 10%
- Baclofen 2%
- Bupivacaine 2% – 5%
- Carbamazepine 5%
- Clonidine 0.1% – 0.3%
- Cyclobenzaprine 1% – 3%
- Dextromethorphan 5% – 10%
- Diclofenac 1% – 5%
- Gabapentin 5% – 10%
- Guaifenesin 10% – 40%
- Ibuprofen 10% – 40%
- Indomethacin 10% – 40%
- Ketamine 5% – 10%
- Ketoprofen 10% – 50%
- Lidocaine 2% – 10%
- Loperamide 1%
- Nifedipine 2% – 16%
- Orphenadrine 5% – 10%
- Phenytoin 2% – 10%
- Piroxicam 0.5% – 2%
- Tetracaine 0.5% – 10%
- Topiramate 1%

Side effects

Patients should be counseled about potential side effects or adverse reactions. While systemic absorption is usually minimal with these ingredients, some is inevitable. For patients with underlying comorbidities—ulcers, asthma, renal
Topical analgesics as alternative first-line agents

impairment, use of anticoagulants—drug-drug interactions or side effects must be considered. Topical NSAIDs have the same systemic warnings as the orally-administered NSAIDs for this reason: there is some absorption into the systemic circulation. The package insert warnings are the same for topical NSAIDs and systemic NSAIDs because not enough is known about the adverse effect profiling, including renal function, for topicals.

General principles

● Use topical analgesics only on healthy, intact skin
● Exception: occasional use of lidocaine jelly in low concentrations on wounds; however, remember that open wounds will absorb medications systemically more than healthy, intact skin
● Never put topical analgesics in the eyes or mucous membranes unless specifically directed to do so (eg, ophthalmologic preparations)
● These drugs cross the placenta: use caution in pregnant or breastfeeding women
● If a patient has an adverse skin reaction, discontinue topical use! Continued use can only worsen the skin reaction
● Do not use heating pads or other applied heat as heat will increase skin absorption
● Stay out of the sunlight
● After applying topicals, do not apply cosmetics, lotions, moisturizers, or sunscreens over the same site; it is unknown how they might affect absorption of the medication
● As with all medications, keep out of the reach of children
● Beware of overdosing: patients have smothered an extremity in lidocaine cream or gel, wrapped it with plastic wrap, and then taped it to try to make the extremity numb
● Do not bandage the area tightly
● Some topical patches have very poor adhesion and require tape reinforcement to keep them on the skin

There is some controversy as to whether someone on an oral NSAID for rheumatoid arthritis, for example, can use a topical NSAID for a focal spot of pain. The systemic absorption from topical NSAIDs is miniscule compared to that of an oral. Therefore, for a younger, healthier patient, it should not pose a problem; these are decisions left up to individual clinicians based on specific patient profiles. To be safe, however, an oral and a topical should not be used concurrently, especially in patients with comorbidities.

Conclusion

Data support the utility of topical analgesics. Like all other therapies, effectiveness may be limited to certain patients, such as those with musculoskeletal or arthritis pain, or inflammatory or neuropathic conditions. The benefits of maximizing opioid sparing and minimizing adverse effects vs systemic analgesics is clear. OTC products can receive FDA approval via the new drug application pathway if data support their claims. Practice guidelines have emerged recommending topical analgesics with or without menthol as first-line agents for the treatment of non-low back musculoskeletal pain. Clinicians should consider the data supporting OTC products when making initial treatment decisions for these patients.

Case studies

Case 1
An 84-year-old female suffered a fall onto her left knee approximately 6 months ago. Imaging reveals advanced degenerative arthritic changes without obvious fracture. She continues to complain of severe pain with standing and ambulation. Her medical history is significant for
hypertension, mild renal insufficiency, and mild dementia. Her primary care clinician will not allow oral NSAIDs, and she suffered with hallucinations and dysphoria on low dose mu opioids. Despite being on a low dose SSRI, she was placed on tramadol without significant benefit. Following failure of multiple analgesic regimens, she had some relief with topical diclofenac gel, an OTC 4% lidocaine patch, and an offloading knee brace. She also began using a cane for ambulatory assistance. Her pain scores have dropped from 10/10 to 4–5/10, and she denies any noticeable adverse effects from her current regimen.

**Case 2**

A 46-year-old construction worker suffered an injury to his left wrist in a work-related accident. He has been using hydrocodone/acetaminophen 5/325, 4 tablets per day on average. He has 2 to 3 alcoholic drinks on most days of the week and describes significant gastritis with use of oral NSAIDs. He failed to benefit from 2 orthopedic corticosteroid wrist injections and wishes to taper off the opioid regimen. He had some benefit from topical capsaicin, but did not appreciate the warmth/burning he experienced. He found relief with a topical menthol/methyl salicylate/camphor patch and a wrap-around wrist support. This allowed him to continue working and maintain his activities of daily living. He was instructed to use lidocaine gel/spray as a PRN rescue analgesic modality.

**References**

Topical analgesics as alternative first-line agents

3 Topical analgesics:

a Usually exceed systemic plasma concentrations
b Have a greater adverse effect profile than systemic agents
c Minimize plasma exposure and potentially adverse events
d Achieve similar concentrations to transdermal agents

4 Compared to many parts of the world, how many topical analgesics does the US use?

a Fewer
b The same amount
c More

5 An 84-year-old female suffered a fall onto her left knee approximately 6 months ago. Imaging reveals advanced degenerative arthritic changes without obvious fracture. She continues to complain of severe pain with standing and ambulation. Her medical history is significant for hypertension, mild renal insufficiency, and mild dementia. Her primary care clinician will not allow oral NSAIDs, and she suffered with hallucinations and dysphoria on low dose mu opioids. Despite being on a low dose SSRI, she was placed on tramadol without significant benefit. Following failure of multiple analgesic regimens, she had some relief with topical diclofenac gel, an OTC 4% lidocaine patch, and an offloading knee brace. She also began using a cane for ambulatory assistance. Her pain scores have dropped from 10/10 to 4–5/10, and she denies any noticeable adverse effects from her current regimen. Risks from oral NSAIDs include all of the following except:

a Renal and hepatic dysfunction
b GI distress and bleeding
c Cardiovascular events (MI and stroke)
d Hypercoagulable/clotting events

Posttest Questions

Below is a preview of the posttest questions. In order to claim credit, please go to https://pain.sh/xuz to complete the online posttest and evaluation.

1 Which of the following organizations have guidelines recommending topical analgesics?

a American College of Physicians
b American Academy of Rheumatology
c Centers for Disease Control
d American Academy of Family Physicians
e All of the above

2 Capsaicin works by:

a Blocking peripheral serotonin
b NMDA receptor antagonism
c Denervating cutaneous nerve fibers following binding to transient receptor potential channel vanilloid-receptor type 1 (TRPV1) receptors
d Blocking calcium channels and depolarization
6. All of the following are true of acetaminophen except:

- a. It is the most common cause of liver transplantation in the US
- b. 50% of reported overdoses are unintentional
- c. It is commonly combined with topical analgesics
- d. It is commonly combined with oral analgesics

7. A 46-year-old construction worker suffered an injury to his left wrist in a work-related accident. He has been using hydrocodone/acetaminophen 5/325, 4 tablets per day on average. He has 2 to 3 alcoholic drinks on most days of the week and describes significant gastritis with use of oral NSAIDs. He failed to benefit from 2 orthopedic corticosteroid wrist injections and wishes to taper off the opioid regimen. He had some benefit from topical capsaicin, but did not appreciate the warmth/burning he experienced. He found relief with a topical menthol/methyl salicylate/camphor patch and a wrap-around wrist support. This allowed him to continue working and maintain his activities of daily living. He was instructed to use lidocaine gel/spray as a PRN rescue analgesic modality. Potential benefits of topical analgesics include:

- a. Opioid and NSAID sparing effect
- b. Tissue concentrations exceed systemic levels
- c. Avoidance of GI issues
- d. All of the above

8. Diclofenac is available in:

- a. Gel and liquid
- b. Oral tablets
- c. Topical patch
- d. All of the above

9. Methyl salicylate works as both a counter-irritant and anti-inflammatory agent.

- a. True
- b. False

10. Topical over-the-counter patches containing menthol and methyl salicylate have data supporting their effectiveness.

- a. True
- b. False