



Prescribing flexibility through prescription compounding

Scott Brown, PD

From the Custom Prescription Shoppe, South Burlington, Vermont.

KEYWORDS:

Compounding
 pharmacists;
 Transdermal gels;
 Pluronic Lecithin
 Organogel

Compounding pharmacists are trained to work closely with health professionals to provide medications that are not commercially available. In the area of pain management, case studies have been used to outline some of the treatment options available for practitioners with compounded medications. A list of transdermal medications and corresponding formulas are provided as a starting point to help with this prescribing process.

© 2008 Elsevier Inc. All rights reserved.

Compounding pharmacists can assist the patients of physicians and other licensed prescribers by providing them with access to unique medications and dosage forms. Pharmacists trained in the art and science of compounding are opening specialty compounding pharmacies to aid those who require individualized medication. A patient in need of a preservative-free medication, a medication that is no longer manufactured, a special dosage form, or perhaps a combination of several medications into one dose can be helped by a pharmacist who specializes in solving medication noncompliance issues.

Compounding case study

Carol, a 75-year-old female, developed pain over her left hip that she described as feeling like “a thousand bee stings.” After much research, the patient found a reference for a topical pain gel containing 6% gabapentin. During a routine office visit with her endocrinologist, the patient asked if she could be given a written prescription for the pain gel. The prescription was prepared by a compounding pharmacist, and the patient applied it a few times daily to the painful hip. The patient described her pain as a “10” on

a scale of 1 to 10 before applying the gabapentin and as an “8” after application. After much consideration, clonidine 0.2% and lidocaine 1% was added to the gabapentin formula. This time after application of the “new” pain gel, the hip pain was scored as a “3” on a scale of 1 to 10. After several months of use, the patient has found that she can apply the “new” pain gel once every 2 or 3 days and stay nearly pain free.

Medical professionals from dentistry, pain medicine, surgery, ob-gyn, and many other medical specialties rely on having access to innovative medication compounding services. One example of the unique services and medications that compounding pharmacists provide is in the area of pain management. Pain medications can be prepared by a pharmacist in a properly equipped pharmacy laboratory. Dosage forms like oral lozenges, topical pain gels (see (Table 1), delayed release capsules, and injections can be formulated by the pharmacist and prescriber to meet the specific needs of the patient in pain. The medication can be compounded at the exact strength required by the patient. Lozenges can be flavored and sweetened to diminish the bitter taste of a drug, or topical pain gels may be applied near the painful muscle or inflamed nerve.

Compounding case study

A 41-year-old female, who complained of chronic pain at the site of a wisdom tooth extraction 7 years previous, was

Address reprint requests and correspondence: Scott Brown, PD, Custom Prescription Shoppe, 42 Timberlane Lane, South Burlington, VT 05403.

E-mail address: scott@customrxshop.com.

Table 1 Medication ingredient list (transdermals)

Medication	Concentration (%)	Use	Reference
Ketoprofen	10-20	Anti-inflammatory	5
Amitriptyline	2	Local analgesia, used with baclofen	6
Gabapentin	6	Local analgesia	7
Ketamine	5-20	Local analgesia	8
Clonidine	0.1-0.2	Local analgesia	9
Lidocaine	1-2	Local analgesia	

referred to us by a dentist. Current oral pain medications included gabapentin, baclofen, amitriptyline, and hydrocodone/APAP. The patient was started on an amitriptyline/carbamazepine/lidocaine gel, which was used in a stent in the mouth. This gel was used for break-through pain. The prescription was changed to a clonazepam/benzocaine gel mixture, which is currently being applied with the fingertip to the painful area. This gel has been very helpful for the patient and is used up to three times daily for pain. Both gels are compounded in the pharmacy laboratory to the dentist's specifications.

Topical pain gels

Transdermally delivered medications can be applied to painful joints, muscles, or directly onto the site of neuropathic pain. Sources of pain can include trauma, surgery, malignancy, arthritis, or any other type of pain that cannot be managed. Topical medications, customized for an individual patient, have been helpful for patients in need of a more personalized approach. Williman and coworkers¹ showed that lecithin organogel can be a matrix for transdermal transport of drugs. Specially prepared emulsions are compounded which penetrate the skin and drive medications into underlying tissue. Some of the drug classes available for topical application include Tricyclics, NMDA antagonists, Anticonvulsants, Alpha-2 agonists, NSAIDs, muscle relaxants, GABA agonists, and anesthetics.

Evidence exists that topically applied pain medications can provide pain relief (Table 1). Peripheral alpha-1 and

glutamate receptors² and opioid and alpha-2 receptors have been identified. NMDA and AMPA receptors in the temporomandibular joint (TMJ) have been reported by Carins.³ Two or more medications with different mechanisms of action can be formulated into a compounded base with penetration-enhancing chemicals. Using pure medication powders obtained from a licensed chemical supplier, the pharmacist dissolves the powders in an appropriate solvent and blends them into a suitable gel base. This preparation is then milled to reduce particle size and to increase transdermal absorption. The final formulation can be dispensed in an ointment jar, a topical syringe, or some other dispensing device.

Transdermal gels have been formulated by compounding pharmacists to deliver both hydrophilic and hydrophobic medications through the epidermal layer of the skin. The transdermal gel consists of the base, a solvent to wet the medications, and the medication(s). Pluronic Lecithin Organogel (PLO) is a base that is commonly used as a transdermal vehicle. PLO is composed of pluronic gel, lecithin, and isopropyl palmitate. Pluronic gel is a surfactant having low toxicity and irritability on the skin, excellent compatibility with other chemicals, high solubilizing capacity for different drugs, and good drug release characteristics. Lecithin acts as a solubilizing agent and spreads well when applied to the skin. Ethoxy Diglycol is a commonly used solvent that is used as a "wetting agent" for the powdered medication(s). A study by Ritschel and coworkers⁴ showed that Ethoxy diglycol, when compared with water as a "wetting agent" for the powdered medication(s), helped to deposit and retain the medication in layers of the skin.

Several companies now manufacture transdermal gels for compounding pharmacists to use when compounding topical pain formulations. Anhydrous gels can also be used as a base, having the benefit of being more stable for medications that react with water.

Table 1 contains a list of some medications that can be compounded into topical pain gels. The prescriber may pick one or more medications from this list when prescribing for a patient. Table 2 is a Treatment Formula Table that lists options for various medical conditions. These are simply suggestions of treatments that have been used successfully in my pharmacy practice.

Prescription compounding services are now available from compounding pharmacists in many communities.

Table 2 Treatment formula table

Medical condition	Medication	Directions
Low back pain/arthritis	Ketoprofen 10-20%, or Ketamine 10%/Ketoprofen 10%	Apply 2-3× per day as needed
Low back pain/Arthritis	Ketoprofen 10-20%/Cyclobenzaprine 1%/Bupivacaine 0.5%	Apply 2-3× per day as needed
Myofascial trigger points	Ketoprofen 5%/Gabapentin 5%/Ketamine 5%	Apply 2-3× per day as needed
Neuropathic pain	Ketamine 10%/Clonidine 0.2%/Gabapentin 6%	Apply 2-3× per day as needed
Herpetic neuralgia	Ketamine 10%/Clonidine 0.2%/Gabapentin 6%	Apply 2-3× per day as needed
Fibromyalgia	Magnesium Chloride 10%	Apply 2-3× per day as needed
CRPS	Lidocaine 10% or Bupivacaine 0.75% spray	Apply 2-3× per day as needed

These compounding specialists can bring relief to acute and chronic pain patients with medications created for individual patients. Prescribers can call or set up an appointment to visit a compounding pharmacist and discuss various options for their prescribing needs.

References

1. Williman H, Walde P, Luisi PL, et al: Lecithin organogel as matrix for transdermal transport of drugs. *J Pharm Sci* 81:871-874, 1992
2. Drummond PD, Skipworth S, Finch PM: Alpha-a-adrenoceptors in normal and hyperalgesic human skin. *Clin Sci* 91:73-77, 1996
3. Cairns BE, Sessle BJ, Hu JW: Evidence that excitatory amino acid receptors within the temporomandibular joint region are involved in the reflex activation of the jaw muscles. *J Neurosci* 18:8056-8064, 1998
4. Ritschel WA, Panchagnula R, Stemmer K, et al: Development of an intracutaneous depot for drugs. Binding, drug accumulation and retention studies, and mechanism of depot. *Skin Pharmacol* 4:235-245, 1991
5. Chi SC, Jun HW: Anti-inflammatory activities of ketoprofen gel carrageenan-induced paw edema in rats. *J Pharm Sci* 79:974-991, 1990
6. Lynch ME, Clark AJ, Sawynok J: A pilot study examining topical amitriptyline, ketamine, and a combination of both in the treatment of neuropathic pain. *Clin J Pain* 19:323-328, 2003
7. Carlton SM, Zhou S: Attenuation of formalin-induced nociceptive behaviors following local peripheral injection of gabapentin. *Pain* 76:201-207, 1998
8. Gammaitoni A, Gallagher RM, Welz-Bossna M: Topical ketamine gel: possible role in treating neuropathic pain. *Pain Med* 1:97-100, 2000
9. Schwartz SI, Allin D, Kipness MS: Dose ranging and tolerance study of 0.05% clonidine gel in patients with painful diabetic neuropathy. Program and abstracts of the 19th Annual Scientific Meeting of the American Pain Society; November 2-5, 2000; Atlanta, Georgia. Abstract 671