

Compounded Drugs of Value in Outpatient Hospice and Palliative Care Practice

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Abstract

A compounded preparation is needed when no commercially manufactured medication is available to adequately address a patient's medical needs. Among the greatest therapeutic challenges faced by both patients and caregivers is the treatment required by individuals who have a terminal condition. We discuss some of the most often prescribed compounds used in outpatient hospice and palliative care to treat common conditions (wounds, pain and dyspnea, intractable cough, nausea and vomiting, depression, bladder infections caused by an indwelling catheter, rectal pain).

Introduction

The journey of dying can be very difficult. At a time when there is increasing interest in patient-centered care, when the patient is considered a person (not "that gallbladder"), and when patients are recognized as having more complex needs than does a widget on an assembly line, it seems appropriate to discuss the value of compounded drugs in treating those patients whose therapy with manufactured drugs has not proven effective. Customized medications, which are prescribed by a physician and designed and prepared by a compounding pharmacist, can provide effective treatment when needed medications or delivery systems are not commercially available.

Compounding pharmacists have a long history of providing safe and effective preparations for prescription from a wide variety of medical specialists, especially those clinicians who treat severe, advanced, or terminal illnesses. In many hospitals, formularies limit the choices of drugs prescribed to treat unusual conditions, and most hospital-based healthcare professionals know little about innovative customized preparations designed to treat a refractory condition in a specific patient. However, because the duration of a hospital stay is usually short term, many patients for whom compounded drugs are most useful are cared for at home. They are usually elderly, have an advanced stage of illness, are frail, and/or have lost the ability to function in essential ways so they must be confined to a chair or bed. Most are ill due to diseases that cause end-organ failure, cancer, or dementia. When family caregivers are no longer able to provide care at home, such patients may be relegated to living in an assisted-living, nursing home, or long-term care facility.

Some of the most problematic issues for physicians and nurses who care for patients with a terminal illness involve treating wounds, pain and dyspnea, intractable cough, nausea and vomiting, depression, bladder conditions caused by an indwelling catheter, and/or rectal pain. In this article, we describe what we have found to be some of the most effective compounded preparations for treating those disorders in outpatients. For physicians, those compounds offer the flexibility to prescribe doses and delivery systems that are designed for individual patient needs. For patients, they provide much-needed relief when commercially manufactured medications are ineffective or cannot be tolerated.

It is difficult to find evidence-based studies on the management of end-of-life conditions because each patient's medical case is unique. In addition, maintaining a controlled environment for such patients is difficult. However, the effectiveness of the compounds we describe in this report is substantiated in the medical literature, by long experience, and by testimonials from or about hospice patients treated with customized medications that eased suffering and improved quality of life. Formulations for the preparations presented in this lecture should be obtained from a compounding pharmacist in your community.

Compounded Preparations for Palliative Care and Hospice Patients

Decubitus ulcers and similar wounds

Wounds like decubitus ulcers often afflict frail, bedridden patients who are unable to care for themselves. There are two types of decubitus ulcers: those that can be healed and those that will not heal. Painful wounds cannot be healed when the condition of the surrounding tissue is poor, the patient is malnourished, blood supply to the area is inadequate, and/or the protoplasm necessary for skin regeneration is insufficient. In those patients, the goal of care is to provide comfort. However, when the condition of the tissue around the wound is good enough to permit regeneration and the blood supply to the injured area is sufficient, both comfort and healing can be achieved. The complete healing of a painful ulcer tremendously boosts the morale of both patients and caregivers. We have found that each of the following compounds offers treatment benefits not provided by commercially manufactured drugs.

Phenytoin paste or gel

Phenytoin paste is frequently compounded to heal decubitus ulcers [1] and other wounds. [2-3] A 5% phenytoin paste is widely used for that purpose in hospice settings. Years ago, physicians noted the overgrowth of gingival tissue in epileptic children treated long term with phenytoin. We now know that that drug stimulates the rapid regrowth of normal tissue in decubitus ulcers and other wounds if the wounded tissue is not irreparably damaged and the blood supply is adequate.

We have found phenytoin to be a consistently effective and relatively inexpensive agent for healing decubitus ulcers, [1] abscesses, [4] vascular leg ulcers, [5] and other wounds [3,5,6] and that it is more effective and less expensive for that purpose than are enzyme or collagenase preparations. Powdered phenytoin 2%, which can be applied with a puffer to a moistened wound, and a 5% phenytoin paste or gel are very effective in healing decubitus ulcers. [7] In 2009, the International Journal of Pharmaceutical Compounding published an article [8] on the successful use of a phenytoin solution to treat giant extremely foul-smelling decubitus ulcers for which no effective treatment had been found. These wounds had developed in patients treated in a military hospital during the Iraq War. In that case, a coauthor of this report (G. M.) collaborated with a military hospital pharmacist and a nutritionist stationed at Camp Bucca, Iraq (the counterpart to Abu Ghraib) to make that treatment possible. Selected letters from their correspondence, which describe the relief of suffering provided by that compound, are included in that article.

Morphine cream

There has been interest in the literature regarding the clinical use of topical opioids for pain relief. [9-11] Morphine cream, which is not absorbed systemically from a denuded surface and is

not effective on intact epidermis or via intact epidermis, can be prescribed to supplement the use of systemic opioids in patients with multiple traumatic wounds, ulcers caused by the complications of diabetes, vascular ulcers due to venous disease of the lower extremities, burns, or wounds that are unusually and/or chronically painful, [12] especially when dressings must be changed. That underused compound is usually effective in relieving the pain of open denuded lesions, and a single application can provide analgesia for 4 to 8 hours. Morphine 1% cream can be applied to an injured area 15 minutes before each dressing change or every 4 hours as needed for chronic pain.

Stanford # 5 oral liquid

Stanford # 5 oral liquid is a compounded combination of medications that relieves the pain and difficulty in eating and drinking caused by mucositis. A painful ulceration and inflammation of the mouth, throat, and/or upper alimentary tract, mucositis is a frequent complication of chemotherapy and radiation therapy prescribed to treat cancer. If used when mucositis persists in palliative care or hospice patients during or after the active treatment phase of cancer, **Stanford #5 oral liquid** helps alleviate pain and aids the healing of that distressing condition. A coauthor of this article (G. M.) compounded **Stanford # 5 oral liquid** for use as a rinse by a hospice patient suffering from chronic mouth lesions. After that patient had used the Stanford rinse for 1 week, she experienced the first relief from that chronic condition in 20 years.

Advanced cancers of the head and neck and neglected, fungating, large cancers of the breast

The management of advanced malignant infected necrotic fungating wounds of the breast, head, or neck is difficult for the professional team, the patient, and the patient's family, especially when foul odors; effusive secretions of pus, mucus, and bloody fluid; pain; and emotional issues exhaust all concerned. Prescribing the following compounds should be considered by every physician who treats a patient afflicted with such a devastating cancer.

Chloramphenicol and metronidazole

For the treatment of large necrotic fungating wounds, a compounded insufflated (puffed) combination of the antifungal agent metronidazole and the antibiotic chloramphenicol in powder form can be more effective than conventional systemic antibiotics and conventional wound care. In an observational trial study that we conducted from 2005 to 2007, 4 patients treated with that preparation by our hospice team experienced a very rapid improvement in their distressing wound symptoms (J.McN. and G.M., unpublished data, 2007). A disposable plastic bellows can be used to insufflate a combination of those drugs directly onto the wound surface in a thin film that must cover the open lesion. The treated wound should then be loosely covered and left undisturbed for 1 to 2 days before the compound is reapplied and the dressing is changed. This treatment produces a striking reduction in odor, purulence, and secretions from wounds. We recommend puffing a thick layer of that compound onto wound surfaces daily, when necessary. Chloramphenicol was chosen for inclusion in the formulation because of its antibiotic effectiveness, the short duration of its required use, and its unlikely systemic absorption. When used as we describe, the benefit of chloramphenicol far exceeds any risk to the patient. Instead of

of chloramphenicol, ciprofloxacin powder has also been used in combination with powdered metronidazole, and that combination is also safe and effective.

Thrombin

Thrombin powder has been used to control blood oozing from wounds like those described above, and that agent can be added to the above-described drugs for administration by insufflation. However, thrombin is expensive.

Monsel's solution

Monsel's solution (ferric subsalicylate), an old and seldom-used compound, [13,14] acts like a styptic pencil to control bleeding. Monsel's solution is very effective when dabbed onto wounds that ooze blood. That compound is also used to control bleeding that develops after slice biopsies and during colposcopy.

Pain and dyspnea

Pain and dyspnea often occur together in patients nearing the end of life, and both are usually treated with commercially available drugs. However, in some instances, atypical dosages or delivery systems are required. In those cases, a compounded formulation can be very effective.

The preparations described below relieve pain and dyspnea very safely and effectively.

Morphine

Having a medication that relieves pain and dyspnea in palliative care and hospice patients is paramount, and the best drug for doing so is morphine. Unfortunately, treatment with morphine has in recent years been compromised by prejudice and misinformation, but that negative image is slowly being overcome. When used in addition to conventional cardiac therapy, morphine is

very effective in relieving shortness of breath and cardiac pain. The efficacy and safety of morphine have been misunderstood by many patients and families, and, sadly, by many underinformed physicians and nurses. Recent studies that stress the value of morphine in treating patients with end-stage congestive heart failure or chronic obstructive pulmonary disease emphasize that morphine does not hasten death but instead allows most such hospice patients to live comfortably until they die. [15-17]

The use of nebulized morphine to relieve dyspnea is controversial. [18,19] That form of morphine is of no benefit to patients with chronic obstructive pulmonary disease or interstitial pulmonary fibrosis but has relieved, sometimes more rapidly than systemic opioids, cancer-related pain in patients with impaired lung function. The benefit of systemic morphine in relieving dyspnea in patients with acute pulmonary edema suggests that nebulized morphine may also benefit patients with severe end-stage congestive heart failure. A compounding pharmacist can prepare, for the prescribing physician, sterile ampules of 2.5mg. or 5 mg morphine sulfate for nebulization.

When pain escalates and the patient is receiving, for example, a sublingual morphine concentrate, using a commercial 20-mg/mL morphine concentrate, it may become necessary for a compounding pharmacist to provide a sublingual customized morphine solution in higher concentrations, up to 60 mg/mL. The sublingual standard dose of morphine used to relieve pain or dyspnea near the end of life is 5 mg every 2 to 4 hours as needed, but depending on the intensity of symptom distress, higher doses at more frequent intervals may be necessary.

Methadone

When all other opioids are not effective, methadone is often the drug needed to relieve intractable pain. [20,21] In patients who are unable to swallow, a concentrated suspension of methadone is not commercially available. It is usually compounded as a 20 mg/ml concentrate for buccal, sunlingual, or oro-pharyngeal absorption and is dispensed in a dropper bottle.

Because methadone is bitter, it is best flavored with a combination of chocolate, raspberry, and mint flavors. Concentrations of 10- to 60-mg/mL can be compounded and dispensed in 15- or 30-mL dropper bottles.

Levorphanol

Compounded levorphanol, which can be prepared in 2- to 8-mg/mL concentrations for oral administration, is an excellent alternative to methadone for pain relief. [22,23] Levorphanol has a stable half-life, exerts no effect on the QTc interval, and is **not** metabolized via type 1 cytochromes. [24] It is compounded most often as a 4-mg/mL oral concentrate suspension with pina colada flavoring and is dispensed in a 30-mL dropper bottle.

Oxycodone and hydromorphone

Either oxycodone or hydromorphone can be compounded in various concentrations for sublingual or oral administration to relieve pain and dyspnea in patients who are unable to swallow. Oxycodone oral concentrate 20 mg/ml is often substituted when the patient is unable to tolerate morphine.

Local and systemic neuropathic pain

Local and systemic neuropathic pain are common in palliative care and hospice patients, and neuropathic pain differs from nociceptive pain. Nociceptive pain includes the more common types of pain that affect the skeletomuscular system, bone, and viscera. Neuropathic pain is

triggered by a different receptor system in the spinal cord and central nervous system that produces lancinating and burning pain. [25,26] Both neuropathic pain impulses and persistent chronic pain impulses activate the N-methyl-D-aspartate (NMDA) receptors in the spinal cord. Neuropathic pain is not controlled effectively by the opioids commonly used to treat pain: morphine, hydromorphone, oxycodone, hydrocodone, and fentanyl.

The three currently available drugs that block the NMDA receptors and are effective in relieving neuropathic pain are ketamine and the opioids methadone and levorphanol. The analgesic effects of methadone and levorphanol have been discussed above. The usefulness of ketamine in providing pain relief is reviewed below. Topical ketamine in particular is very effective in alleviating pain caused by open wounds, and by referred pain from bone, muscle, or internal organs invaded by cancer or damaged by disease or trauma.

Ketamine

One of the most effective agents used to treat local and systemic neuropathic pain is the non-narcotic NMDA receptor antagonist ketamine, which has a long history of use in hospitalized patients. In those individuals, ketamine is usually administered intravenously in subanesthetic doses for several days to overcome neuropathic pain not alleviated by conventional opioids. However, the adverse effects produced by ketamine have limited its use in hospitalized patients, and intravenous ketamine is not available for — or practical for — use in the home setting. Over the past 4 years, other formulations of that drug has been extensively studied as an analgesic, and it has been found that oral ketamine is effective in reducing neuropathic pain in outpatients, in whom it causes only minor adverse effects. [27]

Compounded oral ketamine (20 mg every 4 hours as a syrup) was prescribed to treat one of the authors of this report (G. M.) for the excruciating pain caused by shingles, which affected the trigeminal nerve and produced extreme discomfort. When combined with 600 mg of ibuprofen daily, that compound provided moderate relief for about 2 hours, but a more effective therapy proved to be a compounded anhydrous gel of ketamine 5% plus gabapentin 4%. That gel produced pain relief better than did the oral ketamine preparation. After 5 days' treatment with the transdermal compound, all shingles-related discomfort had resolved. Although that was the experience of only one individual, the resolution of pain resulting from treatment with anhydrous ketamine gel was dramatic.

Transdermal ketamine in a 5% or 10% gel (with or without added gabapentin, clonidine, or lidocaine) is also effective in relieving or reducing somatic pain when applied locally to painful body sites, including the perineal and anal regions. In addition, ketamine has been reported to be an effective analgesic when administered intramuscularly, transdermally, or intranasally for the treatment of pain, and those findings have engendered multiple ongoing scientific studies and much interest in the scientific community. [28,29]

Depression

Providing truly good medical care requires that the spiritual, emotional, physical, and psychological needs of every patient be adequately addressed. To enable that comprehensive and care, physicians and compounding pharmacists must establish a rapport with the patient and the patient's family so that those professionals can call upon their entire armamentarium of therapies to make the end-of-life journey easier. Emotional and psychiatric conditions such as anxiety,

agitation, depression, dementia, and delirium, which can profoundly and negatively affect the quality of life of hospice and palliative care patients, are often inadequately treated.

Ketamine

The rapid and prolonged duration of relief of major depression in cancer patients has recently been reported to be an effect of orally or intramuscularly administered ketamine. [30-34]. As we described in a case report, [27] the remarkable relief of chronic pain, depression, and anxiety in a 44-year-old male hospice outpatient was initiated by a single test-dose of subcutaneous ketamine and was maintained for 11 weeks with a daily dose of oral ketamine (0.5 mg/kg) dispensed as a flavored syrup (40 mg/5 mL). Prior treatments prescribed to resolve this patient's pain, anxiety, and depression had proven ineffective. That patient received a low dose of a benzodiazepine (lorazepam 0.5 mg) 30 minutes before ketamine administration to minimize the mild adverse effects of low-dose oral ketamine. In our opinion, the lessening of depression in this patient could not be attributed solely to the results of effective analgesia. The improvement in his quality of life that resulted from treatment with oral ketamine was a true therapeutic triumph.

Studies in progress will provide more guidance about the novel uses of ketamine, the rapidity and effectiveness of which rival the rapid effects of methylphenidate (Ritalin) in relieving end-of-life depression. In patients with a terminal illness, conventional antidepressant and anxiolytic agents often take too long to become effective. In such individuals, both methylphenidate and ketamine have been reported to have a positive effect within 24 hours after their administration.

Intractable cough

A persistent irritative nonproductive cough can exhaust patients nearing the end of life. When usual treatments for a persistent cough due to cancer, chronic lung disease, or heart disease fail, nebulized lidocaine may help. In such patients, a compounded lidocaine 1 mL of a 2% sterile solution, added to 3 mL of sterile saline, prepared in a sterile environment, can be administered with a nebulizer every 3 to 4 hours. Alternatively, 1 mL of lidocaine can be withdrawn via syringe from a commercially manufactured 20-mL vial of that drug and placed in a nebulizer with 3 mL of normal saline from a sterile prepackaged vial.

Nausea and vomiting

Vomiting and nausea, which are common in patients with a terminal illness such as cancer or congestive heart failure, affect the upper gastrointestinal tract because the function of the liver, pancreas, or gastrointestinal tract is often compromised as the disease progresses. In addition, some such patients experience cortical-induced nausea associated with aversion to colors, tastes, or odors. For patients with nausea and vomiting that is not ameliorated by treatment with commercially available drugs, the compounded preparation HABR (haloperidol [Haldol], lorazepam [Ativan], diphenhydramine [Benadryl], metoclopramide [Reglan]) is often very effective. HABR combines four drugs in one dosage form, which is an advantage for the patient. Each of those agents affects a different receptor system involved in producing nausea and vomiting. The receptor systems acted upon by each drug are listed below, and those systems and drugs act synergistically to reduce or relieve nausea and vomiting.

-- Haloperidol acts on the chemoreceptor trigger zone (CTZ) and dopamine.

-- Lorazepam affects the brain cortex.

-- Diphenhydramine acts on histamine receptors and the CTZ and blocks the extrapyramidal adverse effects of haloperidol.

-- Metoclopramide increases gastrointestinal motility and acts on the CTZ and on dopamine and serotonin receptors.

The usual combination of the active agents in HABR in any dosage form is as follows:

haloperidol, 1 mg; lorazepam, 1 mg; diphenhydramine, 25 mg; and metoclopramide, 5 mg. If necessary, the amount of haloperidol or lorazepam can be reduced to 0.5 mg, or 1 or 2 mg of dexamethasone (Decadron) can be added for its anti-inflammatory effect to the HABR combination.

HABR can be compounded as a short-acting capsule, a long-acting capsule, a suppository, or a liquid. The effectiveness of transdermal HABR in relieving nausea and vomiting is a topic of current investigation. A hospice patient in our care was experiencing projectile vomiting that no other medication had been effective in relieving. We compounded an HABR capsule in the strength described above, and that patient experienced an almost immediate cessation of vomiting after having received the first dose.

Catheter-associated bladder conditions

Many bedbound patients are fitted with an indwelling catheter, which allows urine to be collected without leaking or spilling, preserves skin integrity, and prevents the need for multiple changes of bedclothes. However, wearing an indwelling catheter predisposes the patient to the development of urinary tract infections, and those devices can become blocked by debris and crystals. The following compound is useful in preventing catheter blockage.

Acetic acid solution

If an indwelling catheter is blocked by infection, then treatment with an antibiotic is usually effective and urine turbidity will clear. If the urine is cloudy and turbid in the absence of infection, then amorphous debris and phosphate crystals are likely to be clogging the catheter tubing. A simple remedy for that condition involves irrigating the bladder with 60 mL of a 0.25% acetic acid solution (i.e., a dilute vinegar solution) once or twice daily for 1 week. That solution should be retained in the bladder for 30 to 60 minutes during each treatment. Within a few days after the initiation of that therapy, phosphate crystals and other debris will often clear.

Rectal pain

Constipation and associated rectal or anal fissures and hemorrhoids often cause discomfort in palliative care and hospice patients, and a bowel laxative program is mandatory for those treated with an opioid. Patients with a gastrointestinal disease may also experience diarrhea-associated irritation of the anal canal, and anal and perianal inflammatory processes can cause irritation and itching. The compounds described below are helpful in treating those conditions.

Rectal Rocket

This special suppository, which is used to treat painful hemorrhoids and anal fissures, contains 2% lidocaine and 1% hydrocortisone in a special design that allows the Rectal Rocket to remain in place in the anal canal without sliding into the rectum; thus the active ingredients can be absorbed directly and gradually into inflamed tissue over night. The contoured front end and the flanged bottom of this suppository enable it to treat external and internal hemorrhoids

simultaneously. A special groove on the side of each Rocket allows intestinal gas to escape. Both immediate-release and extended-release Rectal Rockets are available. Five years ago, we compounded a Rectal Rocket for a patient scheduled to undergo surgery to treat an anal fissure. After she had used that therapy for 21 days, the fissure resolved and her surgery was cancelled. The fissure never recurred, but we compounded the same formulation in Rectal Rocket form to effectively heal a rectal fissure in that patient's sister.

Ketamine gel

As we mentioned previously in this article, ketamine 5% or 10% gel, which can be compounded to include either clonidine or gabapentin, can be applied topically to areas of pain and sensitivity to minimize discomfort. When applied to anal fissures and wounds and external hemorrhoids, ketamine in that dosage and form is effective in reducing pain when applied twice daily.

Morphine cream

Morphine 1% cream is also effective in reducing the pain from anal and perirectal lesions and wounds such as decubitus ulcers when applied as needed 2 or 3 times daily with a gloved finger.

Conclusion

Compounded preparations are necessary when a patient's signs and symptoms are not adequately controlled with a manufactured drug because the commercial preparation is not effective, cannot be tolerated, or is inappropriate in the available dose or dosage form. In such cases, clinicians should consider the use of a pharmaceutical compound that is similar to a required commercial drug but can be prepared in a dose or delivery system that better serves the patient's needs.

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Formulations

[Kari, Could you plz. correctly align the content of the Formulations?]

Stanford # 5 Oral Liquid

For 500 mL

Ingredients

Nystatin, USP, powder		0.945 g
Triamcinolone acetonide micronized powder		0.5 g
Chlorpheniramine maleate powder		0.1 g
Tetracycline HCl powder		6 g
Deoxy-D-glucose powder		0.5 g
Simethicone, USP, liquid		10 mL
Flavor, cherry concentrate		15 mL
Water, distilled		25 mL
Master Suspension formula	qs	500 mL

Note: This formula is for nystatin assayed at 5000 U/mg. If the assay is different, then the amount of nystatin used must be adjusted.

Method of Preparation

1. Weigh the powders listed above and levigate in a mortar.
2. Add the distilled water in small amounts to the mortar containing the above-listed powders and mix until a smooth suspension results. Add the simethicone and mix well.
3. Transfer the mixture to a large beaker.
4. Add the flavor and bring to final volume by adding the Master Suspension formula.

Packaging

Dispense in an amber-colored prescription bottle and attach a “Refrigerate” label.

Labeling

Swish and swallow 1 tsp 4 times daily.

Stability

A beyond-use date of 30 days should be assigned to this preparation.

Storage

Refrigerate.

Use

Used to heal mouth lesions and aphthous ulcers; also has an analgesic effect on those wounds.

Quality Control

Use organoleptic methods including sight, taste, and smell.

Master Suspension Formula

For 100 mL

Ingredients

Xanthan gum powder		0.2 g
Sodium benzoate powder		0.1 g
Sodium saccharin powder		0.5 g
Citric acid anhydrous fine powder		0.1 g
Stevioside powder extract		0.2 g
Water, bacteriostatic paraben preserved	qs	100 mL
Sodium hydroxide 20% solution		qs, dropwise, until the needed pH is reached

Method of Preparation

1. Dissolve the sodium benzoate, sodium saccharin, citric acid, and stevioside powder extract in 90% of the total volume of the bacteriostatic preserved water.
2. Add the xanthan gum gradually so that the mixture does not clump.
3. Mix with a spin bar and stir until the suspension is uniform. That suspension should be left mixing for 24 hours to ensure complete hydration.
4. Use the bacteriostatic paraben preserved water (please see the following formulation) to bring the suspension to volume.
4. Add the 20% sodium hydroxide, dropwise, to adjust the pH to a range of 4.5 – 5.0.

Packaging

Store in an amber-colored prescription bottle and place in the refrigerator.

Labeling

Shake well and refrigerate.

Stability

A beyond-use date of 30 days should be assigned to this preparation.

Storage

Store in the refrigerator.

Use

Pharmaceutical necessity.

Quality Control

Use organoleptic methods including sight, smell, and taste.

Bacteriostatic Paraben Preserved Water

For 100 mL

Ingredients

Methylparaben powder		0.525 g
Propylparaben powder		0.0263 g
Water, purified	qs	100 mL

Method of Preparation

1. Heat the purified water to 70°C – 90°C.
2. Using 90% of total volume of water, add the methylparaben and propylparaben powders gradually, with stirring, until those powders have completely dissolved.
3. Let the resultant mixture cool and then use the purified water to adjust the mixture to the volume required.

Packaging

Store in an amber-colored prescription bottle.

Labeling

Bacteriostatic paraben preserved water for formulations where “paraben preserved water” is called for.

Stability

A beyond-use date of 30 days should be assigned to this preparation.

Storage

Store at room temperature.

Use

Pharmaceutical necessity.

Quality Control

Use organoleptic methods including sight, taste, and smell.

Sodium Hydroxide 20% Solution

For 100 mL

Ingredients

Sodium hydroxide pellets	20 g
Water, sterile for irrigation	80 mL

Method of Preparation

1. Gradually add 20 g of sodium hydroxide to 80 mL of water for irrigation with mixing.
2. Add the **sterile** water for irrigation to produce the total volume required.

Note: Solutions of alkali hydroxides absorb carbon dioxide when they are exposed to air. Such solutions should be freshly prepared each time. Carbon dioxide free water can be prepared as follows: Boil purified water or water for irrigation for 20 minutes, transfer to an air-tight glass bottle, and allow to cool.

Packaging

Store in an amber-colored glass dropper bottle.

Labeling

Caustic/corrosive liquid; do not swallow or allow contact with skin. Immediately use water to wash this preparation off the skin if contact accidentally occurs. It is best to use this compound immediately. Discard this preparation after 24 hours.

Stability

A beyond use-date of 24 hours should be assigned to this preparation.

Storage

Store at room temperature.

Use

Pharmaceutical necessity.

Quality Control

Use organoleptic methods including sight and careful smelling.

Morphine Sulfate 1% Emollient Cream

For 100 g

Ingredients

Morphine sulfate powder		1 g
Glycerin		2 mL
Base, emollient cream	qs	100 g

Method of Preparation

1. Make a paste of the morphine powder and glycerin.
2. Add, in geometric proportions, the emollient cream base to the paste made in step 1.

Packaging

Dispense in an ointment tube or a syringe.

Labeling

Two to 4 times daily, irrigate the wound to clean it and then apply either 1 mL of the cream or enough cream to cover the wounded area.

Stability

A beyond-use date of 180 days should be assigned to this preparation.

Storage

Store at room temperature.

Use

Used to alleviate local pain caused by bedsores, pressure sores, or decubitus ulcers.

Quality Control

Organoleptic methods including sight and smell.

Ketamine 10%, Gabapentin 6%, Clonidine 0.2%, Lidocaine 2% Powder

For 100 g

Ingredients

Clonidine HCl	0.22 g
Ketamine HCl	11.5 g
Gabapentin	6 g
Lidocaine	2 g
Ethoxydiglycol	10 mL
Lecithin-isopropyl palmitate solution	22 mL
Pluronic F-127 (poloxamer 407) 30% gel	qs 50 mL

Method of Preparation

1. Triturate the clonidine HCl, gabapentin, lidocaine, and ketamine HCl together. Add ethoxydiglycol to the powders and mix to wet.
2. Add the product of step 1 to the **lecithin-isopropyl palmitate solution** and mix well.
3. Add the Pluronic 30% gel (a qs amount) in small increments to bring to volume.
4. Pass the resultant mixture through an ointment mill.

Note: One milligram of ketamine activity equals 1.15 mg of ketamine HCl, and 1 mg of clonidine activity equals 1.1 mg of clonidine HCl.

Packaging

Dispense in 60-mL syringes.

Labeling

Apply to the affected area to produce a local effect or to the spinal area of the affected nerves to produce a systemic effect every 4 hours to treat neuropathic pain.

Stability

A beyond-use date of 30 days should be assigned to this preparation.

Storage

Store at room temperature.

Use

Used primarily as an adjuvant to treat neuropathic pain.

Quality Control

Use organoleptic methods including sight and smell.

Ketamine 40 mg/5-mL Solution

For 100 mL

Ingredients

Ketamine HCl	0.92 g
Glycerin, USP	25 mL
Stevia concentrate (500 mg/mL)	0.2 mL
Flavor, bitterness suppressing	1 mL
Flavor, chocolate	1 mL
Flavor, raspberry	3 mL
Flavor, peppermint oil	1 gtt
Sorbitol solution	25 mL
Water, bacteriostatic paraben preserved	qs 100 mL

Method of Preparation

1. Dissolve the ketamine HCl in 25% of the total volume of bacteriostatic paraben preserved water.
2. Add the all the flavors and sweeteners. The patient's preferences for other flavors can be accommodated.
3. Add the glycerin.
4. Bring to volume by adding the sorbitol.

Note: One milligram of ketamine equals 1.15 mg ketamine HCl.

Packaging

Dispense in an amber-colored oval prescription bottle.

Labeling

Dose 2.5 to 5 mL every 4 to 6 hours, depending on the patient's need.

Stability

A beyond-use date of 30 days should be assigned to this preparation.

Storage

Store at room temperature.

Use

Nominally used as an anesthetic but is also useful in treating local and systemic neuropathic pain and depression.

Quality Control

Use organoleptic methods including, sight, smell, and taste.

ABHR 1-mg, 25-mg, 1-mg, 5-mg per 5-mL Suspension

For 100 mL

Ingredients

Lorazepam powder	20 mg
Haloperidol powder	20 mg
Diphenhydramine powder	500 mg
Metoclopramide powder	100 mg
Stevia concentrate solution (500 mg/mL)	1 mL
Sodium saccharin concentrate solution (30 mg/0.1 mL)	0.2 mL
Flavor, vanilla	1 mL
Flavor, marshmallow	1 mL
Flavor, vanilla butternut	0.6 mL
Flavor, English toffee	0.6 mL
Sodium chloride, granular [[[Not mentioned in Method of Preparation]]] 100 mg	
Glycerin, USP, natural	1.6 mL

Syrup, simple

100 mL

Method of Preparation

1. Grind all the powders together in a mortar.
2. Wet the resultant mixture with the glycerin to make a paste.
3. Add the sweeteners and all the flavors. The patient's preferences for flavors can be accommodated.
4. Bring to volume with the simple syrup.

[Which wording should we use to add "sodium chloride, granular" to the Method of Preparation?]

Packaging

Dispense in an amber-colored oval prescription bottle.

Labeling

One tsp 2 to 4 times daily, depending on the patient's needs, to control nausea and vomiting.

Stability

A beyond-use date of 30 days should be assigned to this preparation.

Storage

Store at room temperature.

Use

To control nausea and vomiting.

Quality Control

Use organoleptic methods including sight, smell, and taste.

Analgesc Rectal Rocket Suppository

For 6 Rectal Rockets

Ingredients

Hydrocortisone, USP, micronized	0.37 g
Lidocaine, USP	0.79 g
Silica gel, micronized powder	0.12 g
Food color, green	0.06 g
Wax, paraffin block	12.8 g
Base, fatty acid base, grated	24.8 g

Method of Preparation

1. Use low heat (60°C) to melt the fatty acid base and the paraffin; do not microwave. Melt the fatty acid base first, and then add the paraffin.
2. Mix the hydrocortisone, lidocaine, **green food color**, and micronized silica gel in a mortar until that mixture is uniform in consistency.
3. Add the product of step 2 to the product of step 1 gradually; prevent clumping. May sift if desired.
4. Pour the mixture into a Rectal Rocket mold and allow the mixture to solidify at room temperature. (*Note:* A syringe and a 13-gauge [i.e., 3.5-inch long] stainless steel needle attached to a 20-mL syringe can be used to draw up the melt and inject it into each mold.) Slightly overfill each mold until a rounded top appears. The melt will settle slightly when dry. Let the melt solidify at room temperature for 30 to 60 minutes. After 60 minutes, place the solidified melt in the refrigerator for 15 minutes.
5. Remove the solidified melt from the refrigerator, carefully pry apart the mold (see the next step before proceeding), and let each Rectal Rocket settle on a paper towel.
6. With the flange at the top of the mold, use your thumbs to push each suppository away from the mold gently until the flange is a slight distance from the mold. Do not exert too much pressure, or the suppository make break. You can also insert the end of your thinnest, smallest spatula to gently pry the flange end away from the mold.

Notes: Each mold must be calibrated before proceeding. Then adjust the amount of bases needed accordingly. Before it is filled, each mold should be lightly sprayed with PAM (ConAgra Foods, Inc., Omaha, Nebraska), a food-grade silicone, or a light mineral oil to facilitate the smooth removal of the suppository from the mold.

Packaging

Place each suppository in a small polyester bag. Place the polyester bags containing the suppositories into a larger amber-colored zip-lock-type bag.

Labeling

Insert 1 suppository rectally up to the flange at bedtime and leave it in place over night.

Stability

A beyond-use date of 180 days should be assigned to this preparation.

Storage

Refrigerate.

Use

Used to shrink and eliminate hemorrhoids.

Quality Control

Use organoleptic methods including sight and smell.

Chloramphenicol 5% with Metronidazole 2% Polyox Bandage

For 30 g

Ingredients

Chloramphenicol, USP, powder	1.5 g
Polyox WSR-301 powder	3.0 g
Methocel E4M powder	25.2 g

Metronidazole, USP

0.6 g

Method of Preparation

1. Mix the chloramphenicol and the metronidazole together and reduce the particle size of the resultant mixture in the mortar.
2. Mix the Polyox (The Dow Chemical Company, Midland, Michigan) and the Methocel (The Dow Chemical Company) together in another mortar.
3. Geometrically incorporate the product of step 1 with the product of step 2.

Note: Dispense with Polyox (The Dow Chemical Company) application instructions.

Packaging

This powder must be dispensed in an accordion puffer with a 4-oz plastic squeeze bottle filled with water for irrigation.

Labeling

Include directions for application. Spray water for irrigation onto the wound and then puff the powder onto that wet surface. Repeat that process 3 times total, one after another per application, for a total of 3 applications of powder. Repeat that application every 12 hours, if that is the recommended protocol. Dress the wound once or twice daily, depending on the recommended protocol.

Stability

A beyond-use date of 180 days should be assigned to this preparation.

Storage

Store at room temperature.

Use

For the treatment of malignant, infected, necrotic, fungating wounds of breast, head, or neck.

Quality Control

Use organoleptic methods including sight and smell.

Levorphanol 4-mg/mL Concentrate Syrup

For 100 mL

Ingredients

Levorphanol powder	400 mg
(levorphanol 2-mg tabs)	(200 ea); can be used if powder is not available
Propylene glycol	15 mL to be used to make a paste of the tablets
Flavor, bitterness suppressing	3 mL
Flavor, pina colada, anhydrous	3 mL
Stevia concentrate (500 mg/mL)	3 mL
Water, purified	27 mL
Syrup, simple qs	100 mL

Method of Preparation

1. Mark the dispensing bottle at the final (qs) total volume with a marker.
2. Grind the tablets into a fine powder or use the active ingredient as a powder.
3. Only if using ground tablets, make a paste with propylene glycol.
4. Add the purified water to make a solution.
5. Add the flavors and sweeteners.
6. Add the syrup to the “qs” mark on the dispensing bottle.

Packaging

Dispense in an amber-colored oval prescription bottle. Add an easy-fill adapter cap and a 1-mL oral syringe to ensure accurate dosing.

Labeling

One milliliter every 4 to 6 hours to control pain.

Stability

A beyond-use date of 30 days should be assigned to this preparation.

Storage

Store at room temperature or refrigerate.

Use

Relief of pain that cannot be controlled with other opiates.

Quality Control

Use organoleptic methods including sight, smell, and taste.

Lidocaine 1% Inhalation Solution 10 mg/3 mL

For 300 mL

Ingredients

Lidocaine HCl powder		1.23 g
Saline, normal, for irrigation		78 mL
Benzalkonium chloride 1:100 solution		1 mL
Water, sterile for irrigation	qs	100 mL

Method of Preparation

1. Dissolve the lidocaine HCl in 30 mL of **normal saline for irrigation**.
2. Add the benzalkonium chloride solution.
3. Bring to volume with the sterile water for irrigation.
4. Under the hood, filter the preparation through a 0.22-micron filter attached to a large syringe.

Note: It is important to remember that 1.23 mg of Lidocaine HCl yields 1 mg of lidocaine base activity.

Packaging

Dispense in 3.5-mL sterile Uni-Dose (Wheaton, Millville, New Jersey) vials.

Labeling

Decant 1 vial into a nebulizer machine and inhale the contents 4 times daily.

Stability

A beyond-use date of 30 days should be assigned to this preparation.

Storage

Store at room temperature.

Use

For the treatment of intractable cough.

Quality Control

Use organoleptic methods including sight and smell.

Monsel's Solution Gel

For 450 mL

Ingredients

Hydroxyethylcellulose-5000 powder	18 g
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For 300 mL

Ingredients

Morphine sulfate, USP		0.25 g
Citric acid hydrous		0.1 g
Water, sterile for irrigation	qs	300 mL

Method of Preparation

1. Dissolve the morphine **sulfate** and the citric acid in 80 to 90 mL of **sterile** water for irrigation.
2. Bring that mixture to volume.
3. Filter the mixture through a 0.22-micron filter into sterile Uni-Dose (Wheaton) plastic vials.

Note: This formulation must be prepared in a sterile environment under a flow hood. (This preparation can be filtered through a 0.22-micron filter that is attached to the end of a 60-mg [or larger] syringe into the sterile Uni-Dose (Wheaton) vial. Using a large-volume filter results in losing too much of the preparation to the filter.)

Packaging

Dispense in 3.5-mL sterile Uni-Dose (Wheaton) vials with a screw cap.

Labeling

Decant 1 vial into the nebulizer machine and inhale the contents 4 times daily.

Stability

A beyond-use date of 30 days should be assigned to this preparation.

Storage

Store at room temperature.

Use

To treat dyspnea.

Quality Control

Use organoleptic methods including sight and smell.

Phenytoin 5% with Metronidazole 1% Ointment

For 100 g

Ingredients

Metronidazole powder	1 g
Polyethylene glycol base (MW, 300), liquid	62.33 g
Phenytoin, USP, powder	5 g
Polyethylene glycol base (MW, 1450), solid	31.67 g

Method of Preparation

1. Triturate the powders together.
2. Melt the solid polyethylene glycol base (MW, 1450) at 55°C and add the polyethylene glycol base (MW, 300) liquid slowly. Let that mixture warm for 30 minutes.
3. Add the powder to the melted bases and stir until uniformly mixed. Let that mixture spin until the melt is clear. Remove the melt from heat and allow it to congeal while spinning. Do not pour hot melt into the final dispensing containers.
4. Levigate the melt on a pill tile, in an unguator, or through an ointment mill to ensure uniform mixing.

Packaging

Dispense in an ointment tube or a syringe.

Labeling

If possible, use normal saline to clean the wound before treatment. Apply 5 g (1 rounded tsp) to a silver-dollar-sized ulcer twice daily.

Stability

A beyond-use date of 180 days should be assigned to this preparation.

Storage

Store at room temperature.

Use

For the treatment of decubitus ulcers, pressure sores, bed sores.

Quality Control

Use organoleptic methods including sight and smell.

Potassium Permanganate 0.01% (1:10,000) Irrigation Solution

For 1000 mL

Ingredients

Potassium permanganate powder		0.1 g
Water, sterile for irrigation	qs	1000 mL

Method of Preparation

1. Place the potassium permanganate powder in 10 mL of sterile water for irrigation and dissolve the powder.
2. Place the resultant mixture under the laminar flood hood.
3. Remove 10 mL of water from the 1000 mL of sterile water for irrigation and discard that 10 mL.
4. Through a 0.22-micron filter, filter the 10-mL **concentrated** solution of potassium permanganate into the 990 mL of sterile water for irrigation. Reseal the top of the sterile water for irrigation container.

Note: This entire procedure must be performed under a laminar hood or in a glove box to ensure sterility.

Packaging

Dispense in the 1000-mL sterile water for irrigation container.

Labeling

Irrigate the catheter per the healthcare agency protocol.

Stability

A beyond-use date of 30 days should be assigned to this preparation.

Storage

Protect from light and store at room temperature.

Use

For the irrigation of indwelling catheters to treat chronic urinary tract infections.

Quality Control

Use organoleptic methods including sight and smell.

Callouts

The journey of dying can be very difficult. At a time when there is increasing interest in patient-centered care, when the patient is considered a person (not “that gallbladder”), and when patients are recognized as having more complex needs than does a widget on an assembly line, it seems appropriate to discuss the value of compounded drugs in treating those whose therapy with manufactured drugs has not proven effective.

For physicians . . . compounds offer the flexibility to prescribe doses and delivery systems that are designed for individual patient needs. For patients, they provide much-needed relief when commercially manufactured medications are ineffective or cannot be tolerated.

Because the duration of a hospital stay is usually short term, many patients at the end of life are cared for at home, and it is our goal to ensure that in that setting they receive the most effective treatment, especially as their health declines and death approaches.

End-of-life care is multifaceted; it does not lend itself to “cookbook medicine,” and people with a terminal illness are among the most vulnerable patients in need of effective and compassionate care.

Box

Letters From the Heart

The Difference That Compounding Can Make

The following letters are testimonials from the families of hospice patients who benefitted from the skill of a knowledgeable physician and an expert compounding pharmacist.

[Kari, The letters mentioned above will be provided in a separate attachment.]

Box

A Chronicle of Healing

The messages below, which are part of an extensive collaboration among an author of this report (G.M.), a military hospital pharmacist, and a nutritionist stationed at Camp Bucca, Iraq, describe the relief of suffering provided by a phenytoin solution that healed giant malodorous decubitus ulcers when all other treatments had failed. Readers can access more about that novel and successful therapy on the *International Journal of Pharmaceutical Compounding* Web site. [1]

Reference

1. Muller G, Hall LA, Stovall A, Peters SH, Vail J. Missives from Iraq: Compounding in the Theatre of War — Phenytoin Solution Heals Severe Refractory Wounds: An Anecdotal Report. *IJPC* 2009; 13(3): 196-213. Available at: <https://www.ijpc.com/>. Accessed January 26, 2014.

----- Original Message -----

From: Linda Hall

To: George Muller

Sent: Wednesday, March 29, 2006 7:34 AM

Subject: Compounding information.

Hello, Dr. Muller,

My name is Linda (Smithwick) Hall, MSA, RD, CD, CNSD. I worked at Slidell Memorial Hospital as a dietitian in 1995, then went on to Charity Hospital in New Orleans. I moved from New Orleans in 2003 and work as a civilian at Harborview Medical Center in Seattle, WA.

I am also an activated Army reservist stationed in Iraq, working with predominantly detained Iraqis. They are not transferred out of theater and thus become long-term-care patients at our Theater Internment Facility (TIF) hospital.

Many have extensive wounds to heal, surgical and decubitus ulcers. We have limited ability to obtain the state of the art pharmaceuticals for wound healing. The clinical pharmacist here with us, MAJ Audrey Stovall, from New York, has read about using topical Dilantin for wound healing. I remembered you and the work you did for the Slidell Hospice patients in using this product. The physician in charge of the care of detainees here is willing to try topical Dilantin. MAJ Stovall is reading and wondering about the best base for suspension of Dilantin. She has many questions that you may be able to help her with.

I hope you are still operating in Lacombe, with a viable business after hurricane Katrina. I have many friends in New Orleans and one in Slidell whose lives were violently shaken and changed by the storm. I was here in Iraq and my heart and prayers went out for all in the area.

I have included MAJ Stovall in this e-mail in hopes that you and she can communicate.

Sincerely yours,

Linda Hall, MSA, RD, CD, CNSD, CPT, SP
Officer in Charge of Nutrition Care Department
344th Task Force Medical
Unit # 60503

APO AE 09375

----- Original Message -----

From: George Muller

To: Audrey Stovall

Sent: Wednesday, March 29, 2006 11:19 PM

Subject: Dilantin

Hi, Audrey,

Linda Hall spoke with and e-mailed me concerning your interest in using Dilantin for healing decubitus ulcers. We have been using this successfully for over ten years on hospice patients and from Linda's description I believe it would be useful in your practice. I am enclosing some of my formulas for phenytoin that we have used. I am not certain what chemicals you have access to so if you would correspond with me, we can try and work something out that would help your patients.

We use the phenytoin base powder and in most instances we make a "paste" using two polyethylene glycol bases. One of the bases is a liquid and the other, a solid. The low-molecular-weight base (base C) is liquid, and the high-molecular-weight base is a solid. This combination seems to work best. The phenytoin is not absorbed systemically from these bases and works locally only. This type of base helps eliminate stinging and burning. The use of the base phenytoin powder rather than the sodium salt also helps eliminate any burning.

The wound should be free from eschar before applying the paste and may be washed with normal saline before applying the paste.

We also have successfully used the powder as a puffed on "bandage." The Polyox in this formula keeps the powder in place and forms a gelatinous type "bandage" when wet with water for irrigation.

If you can't acquire the chemicals maybe we can help. If you don't have the equipment to make the paste, I may be able to help there also. I belong to a large network of compounding pharmacists who can come to your assistance.

Let me know what I can do to assist you.

Sincerely,

George Muller

----- Original Message -----

From: Linda Hall

To: George Muller

Cc: Valerie Steger

Sent: Saturday, May 13, 2006 12:52 AM

Subject: Progress and Thank you

Dear George,

There was progress utilizing the topical Dilantin using the 100 mg phenytoin sodium dissolved in 5 mL of normal saline. The progress was quite remarkable for most wounds. There was one 17-year-old detainee with stage IV decubiti. These improved to ~ stage II prior to his discharge to Baghdad to be considered for compassionate release. He had one wound with a necrotic center that was not débrided, and as you instructed, the Dilantin did not improve the necrotic area. This was a teaching point for the nurses and physicians (both family medicine and 2 surgeons).

The two surgeons and the family medicine physician were amazed at the effectiveness of the therapy. MAJ Stovall discussed the process with our counterparts the 21st CSH out of Fort Hood. Our hopes is that they will continue the process.

The nurses never staged the wounds. I became the teacher providing literature on how to correctly assess wound stages. They took pictures but never formally documented . . . ! We proceeded without this essential piece of documentation. So, I have subjective eyewitness improvement of the effectiveness of the therapy. The nurses and physicians who also witnessed the improvement now have another effective treatment for wound healing.

In theater, it was impossible for our pharmacist to get topical debridement supplies. This would have been helpful for the necrotic areas. Surgical debridement was the only option.

I hope to visit when I go to New Orleans for a visit, hopefully before the end of this year. You played a large role in the wound care of our Iraqi detained patients. May God richly bless you. I will not have consistent Internet access after today until I return home. I am including the dietitian who is my successor as a point of contact in case the 21st CSH pharmacist wants to contact you.

With respect and appreciation,

Linda

----- Original Message -----

From: Linda Hall

To: George Muller

Sent: Saturday, May 20, 2006 1:09 AM

Subject: Fwd: Re: Fwd: phenytoin package

Dear George,

. . . . We had little pharmacological resources to use other than the Dilantin topically. We were limited because theater health care was governed by trauma care. Detainees were medically classified as trauma, acute, then LTC. Formularies did not keep up with the change. As usual, systems change as impacted by current needs. The beds @ the trauma/critical phase were hospital cots, hard as a tight cot, not helpful for prevention of pressure ulcers, once the detainees were stabilized, then sent to us for acute--> LTC, they came in with stage III to IV ulcers. At Camp Bucca, TIF Hospital beds with foam mattresses were procured in November. There were not enough egg-crate mattresses to keep up with needs; no hydrocolloids at first, then not enough to keep up with needs; no enzymatic topicals; only surgical debridements. One detainee had been with us before we arrived; he had stage IV decubiti; with a wound-vac [the] decubs improved from a [stage] IV to a III. The topical Dilantin solution was started prior to our departure based on the dramatic improvements in the ulcers and wounds of the other wounds this was trialed on. CPT Burch, the physician who had the courage to try the treatment and write orders for it, came to me and said "the topical Dilantin is working, thank you." The two surgeons with us also were amazed at the results; subsequently, the order for topical Dilantin on the stage III and IV wounds that the wound-vacs were working on for greater than 3 months. The 21st CSH, our replacements, will continue the treatments.

Dr. Muller, you have shared your expertise with so many; we are indebted, appreciative, and humbled by your true spirit of caring. . . .

Respectfully yours,

Linda Hall,
CPT, SP, USAR
344th Task Force Medical

Unit #60503
APO AE 09375

[Kari, At the bottom of the last letter, please add: Messages reproduced courtesy of the *International Journal of Pharmaceutical Compounding.*]