Compounding Pharmacists Provide Customized Care

Jennifer Burch

Compounding is the creation of a pharmaceutical preparation by a licensed pharmacist to meet the unique needs of an individual patient when commercially available drugs do not meet those needs. For hundreds of years, compounding was the traditional practice of pharmacy. Today's advanced practice of compounding provides health care practitioners customized options for unique patients or for hard to treat conditions.

Compounding pharmacy is a specialty part of pharmacy practice and essential to the provision of health care in the 21st century. Compounding is the art and science of preparing a customized medication to meet a patient's need that is not otherwise commercially available. From the time of Hippocrates until the 20th century, all prescriptions, including preparations such as plant extracts, pills, and ointments ("salves"), were compounded. Compounding declined in the 1950s and '60s with the onset of drug manufacturing. The "one size fits all" commercially produced medications did not meet the needs of some patients. The resurgence of compounding began in the '90s as patients and health care providers turned to personalized medication options to achieve optimal therapeutic outcomes. Compounding has also helped alleviate drug shortages, non-sterile and sterile, within the health care system in the past 10 years. Compounding occurs across all pharmacy practice settings such as community pharmacy, hospital pharmacy, long-term care, and nuclear pharmacy. Almost every medical specialty, including veterinarians, uses compounded preparations for their patients.

In a 2012 National Community Pharmacy Survey, it was reported that 85.5% of community pharmacies provided some type of compounding [1]. In today's regulatory environment this number is declining. Compounded medications account for just 1-3% of all medications dispensed in the US [2]. Currently, all compounded medications are patient specific and based on a health care provider's prescription.

Compounding-only pharmacies specialize in the preparation of custom medications. The number of compounding pharmacies providing sterile medications has declined drastically in North Carolina and across the country, in part due to both increased inspection activity/enforcement by state boards of pharmacy and pharmacies exiting the market due to increased cost of compliance with sterile guidelines. These specialty practices must have the appropriate space, equipment, trained staff, and commitment to provide compounding to their patients and providers.

Clinical Compounding

Compounding may be as simple as crushing tablets to make a suspension for a child or adult who cannot swallow tablets, or for administration down a nasogastric tube. It may be as simple as adding an additional ingredient to a commercially available cream. Many times, however, it is not that simple.

Professional compounding is not just diluting existing medications or mixing powders with bases. The pharmacist must consider the physical and chemical properties of each active and inactive ingredient to prepare an effective and safe customized medication with the desired taste, color, fragrance, viscosity, uniformity, texture, and stability. The efficacy of any compounded medication is influenced by the technique and equipment used in preparing the formulation, the purity and quality of the ingredients, the choice of vehicle (base), and the proper use of additives such as penetration enhancers. Often a prescriber will have an idea about a unique combination to treat a certain condition in a patient, but that drug is not commercially available. This prescriber will then call a compounding pharmacist to discuss the feasibility of making the compound. Since there are many factors that must be considered before putting a new formula together, the compounding pharmacist plays a vital role.

Table 1 provides just a few examples of what compounding pharmacists can prepare or areas where they can provide alternatives. There are many other unique preparations and delivery systems that are available.

Policies and Procedures

The North Carolina Board of Pharmacy (NCBOP) licenses compounding pharmacies and pharmacists. North Carolina-based pharmacies are inspected annually by the NCBOP.

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TABLE 1.
Commonly Prescribed Compounded Medications

Specialty	Treatment
General	Removal of preservatives, colors, excipients (such as alcohol or lactose), or known irritants (such as parabens, mineral oil, or propylene glycol)
Clinical trials	Provide small batches of capsules that may be blinded or placebo-matched depending on the trial design
Dermatology	Acne, hyperpigmentation, and scar formulas
Pediatrics	Customized liquids for small dose requirements such as for seizure or ADHD medications; transdermal nausea agents such as ondansetron or promethazine; diaper rash formulas
	Ophthalmology: fortified eye drops such as vancomycin, gentamicin, or tobramycin (sterile); autologous serum eye drops (sterile)
Orthopedics/Pain Specialists	Transdermal pain medications such as ketoprofen, gabapentin and/or lidocaine; ketamine nasal spray or capsules for pain in lieu of opiates or to reduce opiate requirements
Psychiatry	Ketamine nasal spray for treatment-resistant depression; compounded medication tapers for anti-depressants or anti-anxiety prescriptions
Urology	Erectile dysfunction intracavernous injections containing prostaglandin, papaverine and/or phentolamine (sterile); customized testosterone replacement therapy
Obstetrics/Gynecology	Progesterone suppositories or progesterone injectable (sterile) for infertility or the support of pregnancy; customized hormone replacement therapies including low dose testosterone; hypoallergenic vaginal cream formulas; non-hormonal vaginal dryness formulas; compounding pharmacists can provide education to patients, testing of hormones, and recommendations to the provider for customized hormone replacement therapies
Gastroenterology	Topical combination medications for anal fissures or hemorrhoids; oral viscous budesonide for eosinophilic esophagitis treatments
Oncology	Transdermal nausea medications; non-hormonal vaginal dryness formulas; mouthwash formulas for mucositis
Podiatry	Combination nail fungus treatments such as fluconazole with ibuprofen; wart removal treatments such as salicylic acid or 5-fluorouracil
Dental	Topical "mucosal bandages" containing steroid and/or anesthetic to cover and protect the ulcerated or infected mucosa; dry mouth lozenges

While compounding is part of most pharmacy school curriculums, pharmacists who do more than basic compounding have had additional training in both the art and science of compounding. I like to think of a compounding pharmacist as a problem solving pharmacist. Often compounding pharmacists and prescribers work together to come up with the best therapy for the patient. This relationship is known as the "triad."

Compounding pharmacists can prepare the following: unique dosage forms containing the ideal dose of medication for each individual; medications in dosage forms that are not commercially available, such as transdermal gels, troches, "chewies," and lollipops; medications free of problem-causing excipients such as dyes, sugar, lactose, or alcohol; combinations of various compatible medications into a single dosage form for easier administration and improved compliance; and medications that are not commercially available.

While compounding pharmacies in North Carolina are overseen by the NCBOP, the Food and Drug Administration (FDA) also has some oversight. In late 2012 there was a compounding tragedy where New England Compounding Center (NECC) in Framingham, Massachusetts distributed contaminated methylprednisolone injections to health care providers and facilities around the country [3]. NECC was responsible for 64 deaths and 753 illnesses due to fungal meningitis. Both the Massachusetts Board of Pharmacy and the FDA had investigated this pharmacy before the tragedy occurred, but had not taken action.

After this tragedy, Congress passed the Drug Quality and Security (DQSA) Act, which was signed into law in November 2013 [4]. This legislation made all compounding patient-specific, meaning each compounded medication now needs an individual prescription for a medication in advance of obtaining the medication, and disallowed "office use" compounding from traditional compounding pharmacies or 503(a) pharmacies. Office use compounding was the practice of sending a medication to the practitioner's office that was to be administered in the office during the course of a patient visit or an in-office procedure. Before the DQSA, if the practitioner needed 20 doses per week of a medication for an in-office procedure, the office could order them in bulk, which did not require individual patient prescriptions. The laws varied state to state around office use compounding.

Patient-specific prescriptions in regard to compounding can create problems for procedures where medication needs are not known until the procedure is underway. Traditional compounding pharmacies in North Carolina are held to the United States Pharmacopeia (USP) <795> (non-sterile) and <797> (sterile) guidelines that describe quality standards for compounding pharmacy practice [5]. USP <795> includes categories of compounding (simple, moderate, and complex) and definitions for terms (eg, beyond-use date, hazardous drug, stability). It also provides criteria for compounding each drug preparation (eg, suitable compounding environment, use of appropriate equipment). USP <797> is the standard for processing, testing, and verifying sterile preparations. It provides guidance on preventing microbial contamination and quality processes for compounded sterile preparations. USP <797> is currently undergoing a major

revision. There are many other USP chapters that are pertinent to compounding and they are referenced throughout USP <795> and <797>.

The DQSA also created another category, known as "outsourcing facilities" or 503B facilities. These facilities can voluntarily register on an annual basis with the FDA as outsourcing facilities, which must adhere to current Good Manufacturing Practices (cGMP) but do not need to receive FDA approval for the medications they compound.

FIGURE 1.
Brittney Muckler, Pharmacy Technician, Prepares a Sterile Preparation

Source. Photographer: Bill Burch

FIGURE 2.
Jennifer Burch, Pharmacist, Measures a Compounded Solution

Source. Photographer: Bill Burch

As with other health care facilities, compounding pharmacies can become accredited. The Pharmacy Compounding Accreditation Board (PCAB), now a service of the Accreditation Commission for Health Care (ACHC) in Cary, NC, was established by 8 of the nation's leading pharmacy organizations in 2007 and is based on the USP standards [6]. PCAB accreditation has rigorous standards and requires up-to-date policy and procedures, annual documentation, demonstrated compliance, and an unannounced inspection every 3 years.

Adequate facilities and equipment are necessary to provide these specialized services. Selection of high quality, USP or National Formulary grade (if available) active pharmaceutical ingredients is also one of the components outlined in the USP and by the FDA.

Choosing a Quality Compounder

Several factors should be considered when choosing to work with a compounding pharmacy/pharmacist. First, is the pharmacy licensed in your state and does it make the type of compound you are looking for? Second, is the pharmacy PCAB/ACHC accredited? If they are accredited, an outside organization has inspected the pharmacy to ensure that quality standards are being met. The ACHC website has a search tool where one can search for accredited pharmacies, http://achc.org/accreditation-locations.html. If the pharmacy is not accredited, you should ask some additional questions.

An online questionnaire called Compounding Pharmacy Assessment Questionnaire (CPAQ) [7], provided by the International Association of Compounding Pharmacists (IACP), offers a list of questions to ask a prospective compound pharmacy. Particular attention should be paid to the areas of internal controls, quality assurance, and testing/verification. Questions should include the following: is the pharmacy licensed in my state? Does the pharmacy comply with state laws? Does the pharmacy comply with USP <795> for non-sterile compounds and USP <797>for sterile compounds? How is compliance demonstrated? How does the pharmacy determine a "beyond use date" (how long the medication should be used)? Does the pharmacy have a quality assurance and continuous quality improvement program in place? Does the pharmacy regularly test potency and/or sterility of their compounds?

My personal bias is to recommend that health care providers work with local compounding pharmacists within their region or state so that they may vet their compounding pharmacy before referring patients to them. Compounding pharmacists do not mind this vetting. Many times, it is an educational experience for a provider to visit the compounding pharmacy and see behind the scenes. These visits create trusting relationships and confidence in the compounding medications being prepared and dispensed. NCMJ

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