

Compounded Medications: Made to Order?

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The concept of compounding medications is not new. In its most broad incarnation, compounded medicines have been around since humans began to develop an understanding of the therapeutic properties of naturally occurring substances. Early societies commonly had one person or a few people who passed on the knowledge of making and using medicinal substances to successive generations.

Compounding was common in the United States through the 1930s, but with the advent of improved manufacturing techniques, this labor-intensive method of production fell from favor. Many pharmacy programs began to decrease the emphasis on compounding courses in their routine required classes in the 1970s; however, pharmacists are legally allowed to compound based on their state license.

What does compounding medications mean today? Compounded substances require a current prescription from a provider, or an established history of the medication being prescribed for a particular patient, if the substance is compounded in advance of a current prescription. The International Academy of Compounding Pharmacists (IACP) defines compounding as “a customized medication prepared by a pharmacist according to a doctor’s specifications to meet an individual patient need. Compounding allows the physician to prescribe a custom-tailored medication that is not available commercially” and emphasizes the triad between patient, physician and pharmacist (IACP, 2003). Compounded medications are those that are not available from manufacturers, are not available in a particular form that may be desired, are medications that are combined and not otherwise available in a prepared combination, and that require a pharmacist to individually mix a batch for a particular patient. A simple example is crushing a medication and creating a suspension for patients with swallowing difficulties. But compounding is not limited to suspensions; the finished product can take many

forms and flavors depending on the patient’s needs.

Not all medications can be compounded under Food and Drug Administration (FDA) rules. The FDA prohibits the compounding of copies of commercially available drugs. Any product that has been found unsafe or pulled from the market cannot be compounded. A substance that the FDA has deemed “difficult to compound” cannot be compounded by a pharmacist. Those substances that can be compounded must be prescribed for a specific patient, be an FDA-approved drug, and listed by the United States Pharmacopeial Convention as a widely used drug substance.

Compounding Pros

Compounded medications offer many benefits to the patient, as well as an extraordinary degree of flexibility in administration routes. Medications can be created in forms that are not practical economically for wide-scale manufacture, due to the small number of patients that would require a specific formulation. A certain form for an individual patient can help ensure a positive outcome and patient compliance with the plan of care. This process also allows for prescription of medications that are no longer commercially available or are not available in forms that meet the needs (or wants) for specific formulations.

Each time total parenteral nutrition is administered to a patient, it must be compounded by a hospital pharmacist to meet that particular patient’s needs. Many intravenous (IV) drugs fall into the “compounded” medication category, simply because each patient may have different dose requirements.

If it can be determined that a patient has an allergy to a particular inert ingredient in a commercially manufactured medication, a compounding pharmacist can custom-make a version that omits that particular ingredient.

The arena of pain control benefits from the option to create compounded medications. Many patients may not be able to swallow or many suffer from nausea when taking narcotic pain medications. Compounding offers the provider the option of converting a prescription for a routine oral narcotic to a patch, gel, ointment, or cream that may be more readily tolerated.

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Providers who routinely care for children may turn to a compounded medication in order to improve compliance. Common medications can be made into different, more tolerable flavors, lollipops, or troches that may be better received than a traditional suspension or tablet. Adult formulations of medications may provide a dose that is too high for a child, and the medication can be made in a dose that is suitable for a young patient.

Home care also benefits from compounded medications. This may involve IV drugs, pain control medications, and topical preparations to treat chronic wounds. Multiple medications can be combined into a single dose and remove the difficulty of swallowing multiple pills.

Dermatology is another area in which compounded formulations of creams and ointments are gaining popularity. As more and more consumers become savvy as to what specific substances are most useful for a particular skin problem, dermatologists are being asked to provide specific lotion "cocktails" to fit the needs and wants of particular patients. Often these lotions will include proportions of cortisone, hydroquinone, and retinoids that are tailored to the skin of a single patient.

Compounding Cons

The FDA Modernization Act of 1997 (FDAMA) defines and limits compounding to protect patients from compounded drugs. Since these substances are manufactured without FDA oversight, there can be additional risks involved; some hospital systems require documentation of informed consent prior to their administration (Young, 2003). However, the FDA currently has no uniform way for adverse event reporting in regards to compounded medications. In some states this is governed only by the state pharmacy board, and few states have regulations that require the patient to be informed when compounded medications are substituted for manufactured ones (Young, 2003).

There are further outstanding issues involved with compounded medications. One of the most noticeable is price. Since these are nonstandard formulations, patients have difficulty with reimbursement or insurance coverage for outpatient prescriptions because there are no National Drug Code ID numbers for any compounded medications. Patients may need to contact insurers prior to having the medication filled to investigate their coverage.

Since a pharmacy might not routinely compound medications, the preparation of these substances should be suspect. The appropriate sterile facilities and policies to insure quality may not be available. There have been recent incidences of death in patients who were administered contaminated compounded medications and recalls of medications that were not prepared sterilely (Young, 2002). It can be difficult to insure quality control, without experience in mixing large batches (Nordenburg, 2000) and due to the fact that compounding is not currently emphasized in pharmacy training programs.

Efficacy and dose accuracy represent additional concerns with compounded medications. Drug companies rigorously test the preparation that becomes available for prescription to insure that the advertised dose is the one that is actually being delivered. Altering the medication from a tablet to an ointment will change these parameters, as the entire mechanism of delivery is different. The medication's onset and duration of action may also be altered in often unknown ways. This can be a particular problem with hospice or pain patients; as the concentration of a drug increases, its stability may decrease and higher doses may only be suitable for a specific delivery system. Many popular tablet or pill medications with well-established efficacy and side-effect profiles have never been tested as topical preparations, and may not have any basis in research for such changes to the existing formula.

The issue of the actual available dose represents perhaps the greatest concern with compounded substances. The bioavailability of a substance can change due to altering the delivery system or combining medications. Medications that are well-absorbed in the stomach may not exhibit a similar absorption when reformulated as a suppository or cream. A change that may seem innocuous, such as changing the flavor of a medication, may alter the stability and availability of a drug. Combining two or more substances may lead to unexpected side effects, unanticipated synergistic effects, or cancellation of the desired effects of any or all of the medications in the "cocktail." Often these substances have little, if any, scientific research to establish their intended use as a compounded remedy for any condition. Medications that have been shown to be effective (or ineffective) individually for a specific condition may have no research to suggest that their efficacy will remain (or improve) if compounded with other substances.

Advertising

In 1998 a specific clause (503a) of the FDAMA was attacked for violating pharmacies' right to free speech. The original version of the law prohibited advertising and soliciting orders for specific compounded products, but this clause also exempted compounded drugs from the usual manufacturing standards and "new drug" approval process (Waltz, Ung, & Allen, 2002). The concern that drove the inclusion of clause 503a in the FDAMA was that pharmacies were becoming "manufacturers" of specific products, as in many cases the production of the substance predated a specific patient's prescription for it. In so doing pharmacies also bypassed the usual FDA path to drug approval and eliminated the costs and time involved with clinical trials to establish the efficacy and value of a compounded preparation.

In April 2002, this clause was struck down by the U.S. Supreme Court, stating that the clause violated the pharmacies' right to commercial free speech. The rationale included the need to strike a

Table 1.
Some Compounded Products and Therapeutic Claims

2% amitriptyline and 2% baclofen gel	Application directly to area of neuropathic pain.
Bio-identical hormones	Optimal hormone replacement; alternative to traditional hormone replacement.
L-arginine cream	Stimulates Graffenberg spot (G spot) and enhances orgasms.
Sildenafil rapidly dissolving tablet	Onset reduced to 10-15 seconds.
Sildenafil suspension	Prevents delayed onset seen with traditional tablet; can use twice a day.
Sildenafil troche	40 mg per troche, available in many flavors; for patients with swallowing difficulties.
Sildenafil vaginal cream	For use in women.
Sildenafil/phentolamine rapidly dissolving tablet	Works better than sildenafil alone.
Tri-estrogen (80% estriol, 10% estrone, 10% estradiol)	Alleviate the symptoms of menopause without facilitating breast cancer.

balance between making compounded drugs accessible to providers and making it possible for pharmacies to inform providers that drugs they may be prescribing are actually compounded versions (Waltz et al., 2002).

Direct-to-the-consumer advertising for compounded substances and compounding pharmacies can be found easily, particularly on the Internet, and particularly in the areas of sexual health and menopause. Some of these products claim to be supported by scientific studies, but references may not be readily available as part of the advertisement. Table 1 shows only a few of the preparations and claims that can be readily found.

Conclusions

The use of compounded medications should be evaluated on a patient-by-patient basis. Compounded substances that are available for outpatient use may be of questionable quality (Coyne, Hansen, & Watson, 2003) and may be effective only due to the "placebo effect." It would seem prudent to choose, and prescribe, medications that have received FDA approval and that have a body of scientific evidence that supports the method of delivery and efficacy for a particular purpose. To do otherwise risks harm to patients, and disappointment for patient and provider alike when the product's claims fail to reflect the product's reality. ■

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