

The Compounding Component



Pharmacists remain at the forefront in their expertise in this health care “art form”



BRYAN SPARKS/POCA

Compounding has been a part of pharmacy basically since the profession began. And there is only one group of health professionals—pharmacists—possessing the knowledge and skills required to compound and prepare medications to meet patients’ unique needs. Extemporaneously compounding safe, effective prescription products for patients who require special care is a pharmacy fundamental.

Pharmacy’s heritage spans some 5,000 years, and centers on the provision of pharmaceutical products for patients. In the early years of American pharmacy, compounded formulas were the primary source for medications. For about 150 years (1800-1950), the American pharmacist’s role was to “mix and make” formulas according to prescriber orders. By the mid-20th century, manufacturers took on a greater role in providing medication therapies, and the demand for compounding pharmacist services declined. The transitional decade was in the 1960s. By 1970, nearly 100 percent of all prescriptions dispensed were commercially manufactured.

In the latter part of the 20th century and into the 21st century, the pharmacist’s role shifted primarily from a drug product distributor to a medication therapy manager, and the responsibility to offer compounded alternatives grew in need. This new paradigm, known as pharmaceutical care, practiced in the community pharmacy, identified a significant non-compliance problem with traditional medications.

As a medication therapy manager, pharmacists were called upon to provide alternatives to assist patients in becoming compliant with the prescribed therapy. It became evident that as the commercially available pharmaceutical therapies increased in pharmacokinetic efficiency, patient compliance became a problem. Because most commercially available medications are limited in available strength, dosage form and flavor, the only means available to patients and prescribers in overcoming non-compliance problems is to rely on customized options.

For more than three decades, compounding had been in a slumber as an alternative to successful medication therapy. However, it became increasingly obvious that prescribers required these services to bridge the gap in therapy options for non-compliant patients. Thus, the compounding pharmacist’s role evolved from “mix and make” to that of a problem-solving specialist. Using fundamental pharmacy knowledge, compounding pharmacists invested time and effort to create dosage form alternatives to enhance therapy compliance for difficult patients. No other health professional is capable of bringing to the pharmacotherapeutic decision making table such concepts as pH, particle size, partition coefficient, protein binding, structure activity relationships, economics and epidemiology to assist a prescriber in overcoming a medica-

tion therapy non-compliance problem. Realizing that such services were available, patients and prescribers alike sought out these specialists to assist them in overcoming compliance problems with traditional commercially available therapies.

The shortage of commercially manufactured products has spurred the growth in the demand for pharmacist compounding services. Such drug shortages can cause significant turmoil in the marketplace. Therefore, prescribers have turned to pharmacist compounders for temporary relief.

There are a number of focus areas that have benefited through customized compounded formulations, including pain management, pediatric and geriatric medicine, wound care, andropause, menopause, sports medicine, dermatology, ophthalmology, sterile products, and veterinary medicine.

DEFINITIONS

The following are definitions of compounding and manufacturing:

Pharmacist Compounding

Compounding is the preparation, mixing, assembling, packaging, or labeling of a drug or device by a pharmacist as the result of a practitioner's prescription drug order or initiative based on the practitioner/patient/pharmacist relationship in the course of professional practice; or for the purpose of, or as an incident to research, teaching, or chemical analysis and not for sale or dispensing. Such compounding also includes the preparation of drugs or devices in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns.

Manufacturing

Manufacturing is the production, preparation, propagation, conversion, or processing of a drug or device, either directly or indirectly, by extraction from substances of natural origin or independently by means of chemical or biological synthesis, and includes any packaging or repackaging of the substance(s) or labeling or relabeling of its container, and the promotion and marketing of such drugs or devices. Manufacturing also includes the preparation and promotion of commercially available products from bulk compounds for resale by pharmacies, practitioners, or other persons.

IMPACT ON THERAPEUTIC OUTCOMES

Through the decades, compounding pharmacy has adjusted to patients' evolving needs. Some barriers to optimal health care, however, stand the test of time. As those hurdles become more resolute, the opportunities and solutions provided by

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compounding pharmacists become even more significant and essential.

Regardless of the constant advancements in medical technology and pharmacotherapy, patients struggle to complete their regimens. A 2003 report published by the World Health Organization says that only 50 percent of patients with chronic disease states comply with treatment recommendations. Complete compliance to short-term therapy may be even more difficult because the temporary disruption of a patient's daily pattern is invasive and inconvenient. Fortunately, pharmacists have the opportunity to improve patient compliance to medication regimens, a notion that has long been upheld and examined. A review of 30 studies published between 1969 and 1994 concluded that, while the styles of communication, means of analysis, and reporting techniques varied, the vast majority of studies showed a distinct and positive relationship between patient-pharmacist communication and patient compliance. After discussion with a patient, a compounded product can be tailored to individual needs to account for daily schedules and habits, preferences, and personal concerns about privacy and confidentiality.

In compounding, it's easier and more reasonable to tailor dosage forms to fit into patients' lifestyles, instead of asking patients to adjust their lives during therapy. For instance, it may be much easier for patients to remember to apply a topical or transdermal cream at bedtime when they may already have a similar habit, instead of asking them to remember to take an oral dosage form. More discreet and "portable" dosage forms, such as troches (lozenges) and topical products packaged in small glide-on or roll-on devices, allow patients to carry medications with them, making multiple daily doses more accessible and realistic. Patients with specific preferences or aversions to tastes can easily be accommodated: palatability of products can be increased by masking the taste of the drug itself, changing the viscosity of the product, altering the response of the taste receptors, and creating complemen-

tary flavors. Most practitioners believe that a more involved patient is a more compliant patient. Patients who are actively involved in the decision making process of their regimens—whether it's as complicated as discerning an appropriate dose based on symptomatology, or as simple as selecting a preferred flavor—are more invested, more educated, and generally more adherent.

If patients expect or have adverse effects from prescribed medications, effective therapy is compromised. Compounded products can offer—to both prescribers and patients—the avoidance of such effects. Patients may be sensitive to common preservatives such as parabens, food dyes such as tartrazine (FD&C Yellow No. 5), or sweeteners like aspartame, yet those chemicals can be found in many commercially available OTC and prescription products. A compounded product can be designed to eliminate such ingredients. Lactose intolerance, for instance, can make it difficult for patients to take the majority of manufactured tablets and capsules, while compounded capsules can be formulated using numerous alternative inert fillers.

Negative reactions can be instigated by a host of causes other than patient-specific sensitivities. They are frequently caused by chemical derivatives produced during first-pass metabolism. Utilizing non-oral routes of administration eliminates such metabolism, which can result in possible decreases of adverse effects and, in some cases, decreased doses of medication. Gastrointestinal upset, a common side effect of oral medications, can range from transient and mild to persistent and hazardous, but can be eliminated by employing alternative dosage forms.

Targeting the drug's action site, instead of relying on systemic absorption and effects, can improve patient outcomes, whether that is "measured" by items such as hospital days, wound healing time, pain rating, and quality of life. Transdermal gels and creams formulated with penetration enhancers allow for local drug delivery for effects at the "site of need." An example of transdermal application is using nifedipine to increase circulation in the feet of diabetes patients. In some instances, numerous medications with synergistic action mechanisms can be incorporated to not only alleviate discomfort, but also treat the problem's cause. For example, arthritic and injury-related joint pain has been treated using transdermal dosage forms that incorporate several analgesics to help alleviate numerous types of pain (such as skeletal, muscular, and neuropathic) along with inflammation decreasing agents. A 1996 study examined ketoprofen drug levels after application to the back, the arm, or the knee. It was determined that systemic ketoprofen concentrations after transdermal application were about 20 times lower than

typical systemic concentrations seen after standard oral dosing. Additionally, systemic concentrations after transdermal dosing were 100 times lower than the local concentration at the application site. These data, along with the adverse effects seen with transdermal dosing (which included only mild, topical effects), lend credence to the concept that the transdermal route is effective in delivering medication directly to action site without incurring systemic effects and consequent adverse effects.

Local therapy can also provide more rapid results with fewer adverse effects. Urethral suppositories, or inserts, can be used to deliver local treatment along with anesthesia and pain control for such ailments as urinary tract infections; urinary muscle spasms and incontinence; and urethral and bladder cancers. For chemotherapeutic agents in particular, the prevention of systemic activity, combined with a more concentrated, local effect, makes such alternative dosage forms ideal for accelerated, improved treatment.

The distinction between doses that provide therapeutic efficacy and doses that cause adverse effects can be faint; manufactured drugs may not offer the ideal dose to match that distinction. Manufactured combination medications can increase patient compliance, but the fixed doses of each ingredient may be limiting. For instance, the total daily dose of a combination hydrocodone and acetaminophen tablet is limited by the acetaminophen component, which may lead to inadequate hydrocodone dosing. By decreasing acetaminophen's quantity in a compounded product, a regimen that optimizes the hydrocodone therapy can be followed. Also, some medications must follow tapered dosing to begin or end therapy or to determine the therapeutic dose. The accuracy and consistency of dosing when tablets are split or broken has long been debated. A 1998 study showed that weight variations between 1,752 split tablets varied by more than 10 percent in 41.3 percent of the tablets, and a variance greater than 20 percent was seen in 12.4 percent of tablets. Compounded dosage forms can overcome all these concerns, since they are formulated for a specific need, and can also be adjusted as required by the patient, symptoms, or disease state.

Through compounding, a pharmacist can exercise knowledge and creativity to augment a patient's health care. Understanding of drugs' pharmaceutical and pharmacokinetic characteristics can generate unique therapies with rational pharmacological foundations. For instance, tamoxifen is a nonsteroidal antiestrogenic drug used primarily for breast cancer treatment. Its known effects include the ability to decrease cell proliferation; alter transcriptional synthesis; arrest cells in the G1 phase of development; and modulate the production of

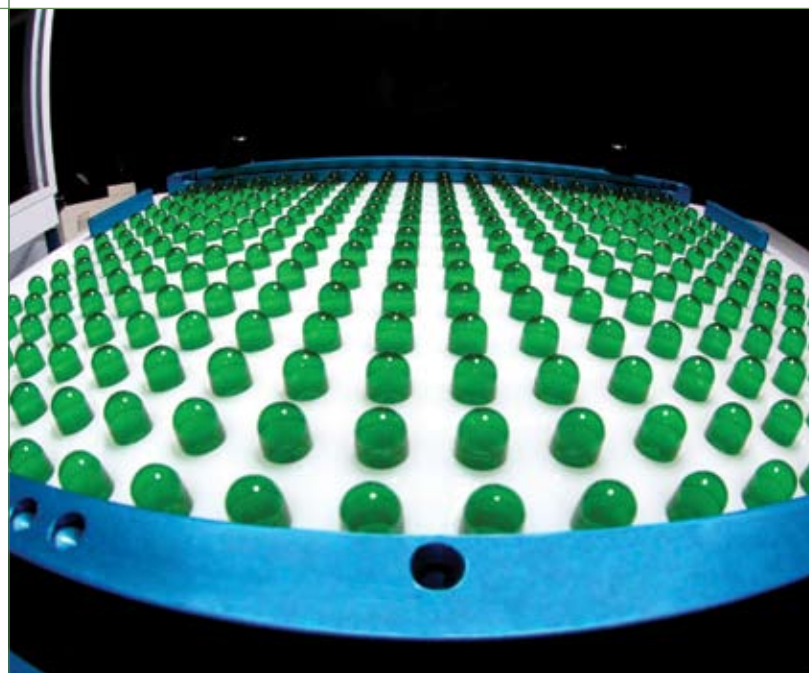
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multiple polypeptide growth factors, including transforming growth factor (TGF) and TGF- β , and epidermal growth factor.

The TGF and TGF- β are known components in the formation of keloid scars. Tamoxifen's down-regulation of TGF- β expression has led to its successful use in the topical treatment and prevention of keloid scars.

Often, patients, physicians and pharmacists work together to achieve a desired outcome with a pharmacologic regimen, only to learn that the central medication has been discontinued by the manufacturer. In some cases, these discontinuations are due to safety concerns; far more often, however, they are prompted by concerns about economic feasibility, patient demand, or issues relating to the large-scale manufacturing process. Drugs that are used to treat small patient populations and transient disease states requiring only short-term therapy are particularly prone to such decisions. In other cases, the chemical itself is not suited to the lengthy procedure of manufacturing, distribution and delivery of the drug to the patient. Chemical properties such as stability, light-sensitivity, and hygroscopic nature may make such extensive processes unfeasible.

Medications that are not pursued by manufacturers remain essential to patients' health care, and the unavailability of those products can greatly alter the quality and even lifespan for those patients. Drugs in pharmaceutical grade chemical form that are still considered safe and effective by the Food and Drug Administration can be obtained by a compounding pharmacist to provide not only that medication, but also a dose, dosage form, and regimen best suited to the patient's needs.



The “traditional” responsibilities of pharmacists are being shifted to other health care professionals: physicians are able to dispense, nursing staff frequently counsel their patients on medication use. Compounding remains as one skill—indeed, one art form—that will not be delegated. As the “team approach” to medical care becomes mainstream, pharmacists are more recognized as an essential member of those teams, and the focus broadens from disease state-specific to whole-patient awareness. Compounded products lend themselves to this perspective because the individualized care of the patient must be all-encompassing. The success of any therapy, especially those that are compounded, relies on the patient/pharmacist/prescriber triad, and specifically, the involvement and participation of the patient. Compounders must act as consultants for both the patient and the health care providers to elucidate and confirm the unique role compounded medications play in medical care. ■

This article was provided by the Professional Compounding Centers of America (PCCA), based in Houston. PCCA provides independent pharmacists with a complete support system for compounding unique dosage forms. For more information about PCCA and its programs, call 800-331-2498 or go to www.pccarx.com.

Editors Note: To obtain the complete list of references used in the article, contact Chris Linville at NCPA (703)838-2680, or at chris.linville@ncpanet.org