The Art, Science, and Technology of Pharmaceutical Compounding

FIFTH EDITION

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Introduction

Pharmacists are unique professionals who are well trained in the natural, physical, and medical sciences and aware that a single mistake in the daily practice of their profession may potentially result in patient harm and even death. However, because of their demonstrated expertise, their demeanor, and the manner in which they have practiced their profession over the years, pharmacists continue to be ranked among the most respected individuals in our society. In general, pharmacists have the reputation of being available to residents of the local community in times of need, interacting with and providing needed medications for patients, and working with patients to regain or maintain a certain standard of health or quality of life.

Pharmacists possess knowledge and skills that are not duplicated by any other profession. Their roles can include dispensing and compounding medications, counseling patients, minimizing medication errors, enhancing patient compliance, monitoring drug therapy, and minimizing drug expenditures.

Pharmacy activities that individualize patient therapy include clinical and compounding functions. The functions are related and equally important to the success of such activities. A pharmacist's expertise must be used to adjust dosage quantities, frequencies, and even dosage forms for enhanced compliance. All pharmacists should be aware of the drug therapy options provided by compounding. Members of the pharmacy profession are united in the belief that they have a responsibility to serve their patients and compound an appropriately prescribed product in the course of professional practice. Pharmacists have both the right and the responsibility to compound medications (sterile and nonsterile) to meet the specific needs of patients.

What Is Compounding?

The definition of compounding has been the subject of much discussion and has been addressed by the United States Pharmacopeia, the standards-setting body for pharmaceuticals in the United States.

Compounding is defined in Chapter <795> of the *United States Pharmacopeia* as follows:

> The preparation, mixing, assembling, altering, packaging, and labeling of a drug, drug-delivery device, or device in accordance with a licensed practitioner's prescription, medication order, or initiative based on the

practitioner/patient/pharmacist/compounder relationship in the course of professional practice. Compounding includes the following:

- Preparation of drug dosage forms for both human and animal patients
- Preparation of drugs or devices in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns
- Reconstitution or manipulation of commercial products that may require the addition of one or more ingredients
- Preparation of drugs or devices for the purposes of, or as an incident to, research (clinical or academic), teaching, or chemical analysis
- Preparation of drugs and devices for prescriber's office use where permitted by federal and state law[1]

The Drug Quality and Security Act (H.R. 3204) defines compounding as "the combining, admixing, mixing, diluting, pooling, reconstituting, or otherwise altering of a drug or bulk drug substance to create a drug."

Compounding may hold different meanings for different pharmacists. It may mean the preparation of suspensions, topicals, and suppositories; the conversion of one dose (e.g., oral to rectal, injection to oral) or dosage form into another; the preparation of select dosage forms from bulk chemicals; the preparation of intravenous admixtures, parenteral nutrition solutions, and pediatric dosage forms from adult dosage forms; the preparation of radioactive isotopes; or the preparation of cassettes, syringes, and other devices with drugs for administration in the home setting.

Compounding occurs in all different types of pharmacies, including the following:

- Independent community pharmacies
- Chain pharmacies
- Hospital pharmacies
- Mail-order pharmacies
- *Compounding-only* pharmacies
  - Independent (human and veterinary)
  - Specialty (home health care, hospital contract, etc.)
- Nuclear pharmacies

Compounding is especially important to select patient-group populations, including those with needs related to pediatrics, geriatrics, bioidentical hormone replacement therapy, pain management, dentistry, environmental and cosmetic sensitivities, sports injuries, and veterinary compounding (small and large animals, herds, exotic and companion animals).

Reasons for the increase in compounding can be related to the following:

- Limited dosage forms
- Limited strengths
- Home health care
- Hospice
- Unavailable drug products and combinations
  - Discontinued drugs
  - Drug shortages
- Orphan drugs
- Veterinary compounding

- New therapeutic approaches
- Special patient populations
- Biotechnology-derived drug products

A pharmacist plays an important role on the hospice team and can greatly enhance quality of life for hospice patients. Pediatric patient compliance is a challenge, because children either do not want or are unable to take tablets or capsules and manufacturers do not provide liquid dosage forms for many medications; this is where a pharmacist steps in. Compounding for the geriatric patient can be a much greater challenge than for almost any other group of patients. Physical, emotional, and social difficulties often affect compliance, and many geriatric health problems are chronic rather than acute. Pharmacists have also become intimately involved in working with veterinarians in the treatment of animals (companion, herd, recreational, food, and exotic).

Compounding has always been a basic part of pharmacy practice; today it continues to be a rapidly growing area, and many pharmacists in all types of practice are becoming involved in compounding sterile and nonsterile preparations. Newly evolving dosage forms and therapeutic approaches suggest that compounding of pharmaceuticals and related products specifically for individual patients will become more common in pharmacy practice in the years ahead.

Approximately 75% of community pharmacists, virtually all hospitals, many chain store and mail-order pharmacies, and many specialty pharmacies compound. Nonsterile or sterile compounding is involved in about 10% of all prescribed and ordered medications today, and compounding is valued up to about $25 billion to $30 billion a year.

Compounding pharmacy is unique because it allows pharmacists to use more of their scientific, mathematical, and technology background than do some other types of practices. Compounding pharmacists develop a unique relationship with the patients they serve. They work hand in hand with physicians to solve clinical problems not addressed by commercially available dosage forms. Ironically, as we in health care become more aware that patients are individuals, respond as individuals, and must be treated as individuals, some health care providers appear to be grouping patients into categories for treatment, for reimbursement from third-party payers, or for a determination of levels of care in managed care organizations. Similarly, the trend toward using pharmaceutical manufacturers' fixed-dose products, which are available just because the marketing demand is sufficiently high to justify their manufacture and production, seems inappropriate. Since when should the availability, or lack of availability, of a specific commercially available product dictate the therapy of a patient?

Should Every Pharmacist Compound?

Only properly trained pharmacists should be involved in pharmaceutical compounding. If pharmacists wish to compound but do not possess the required techniques and skills, they should participate in continuing education programs that have been designed to provide the proper training, including the scientific basis and practical skills necessary for sound, contemporary compounding. Today, any pharmacist is legally qualified to compound, but not all are technically qualified and trained to be a compounding pharmacist. To be capable of meeting the special or advanced needs of today's patients, whether human or animal, a compounding pharmacist must

- Have access to the most recent information available,
- Maintain an inventory and provide for proper storage of drugs and flavoring agents and be capable of obtaining any chemical within a reasonable time,

- Be dedicated to pharmacy and willing to put forth the necessary financial and time investment,
- Have the appropriate physical facilities and equipment to do the job properly (the extent and type of compounding may be determined or limited by the facility),
- Be committed to lifelong learning and continuing education, because a major advantage of compounded prescriptions is their provision of treatments that are new, undeveloped, and often not commercially available, and
- Have a willingness to tear down walls and build bridges to share experiences with others for the good of all.

Should You Compound?

When considering whether or not to compound, pharmacists should consider the technical aspects and economic effect of the service. A new chapter has been added to this edition of the text, "Pharmaceutical Compounding Errors," Chapter 33. The purpose of this chapter is to assist in making one aware of potential errors that can occur in compounding.

Technical Considerations

There are three types of compounded prescriptions: isolated, routine, and batch prepared. An isolated prescription is one that a pharmacist is not expecting to receive and does not expect to receive again. A routine prescription is one that a pharmacist may expect to receive on a routine basis in the future; there may be some benefit in standardizing such preparations (maintaining preparation protocols on file) to ensure product quality. A batch-prepared prescription is one that is prepared in multiple identical units as a single operation in anticipation of the receipt of future prescriptions.

Pharmacists must consider not only their technical qualifications to compound a preparation, but also the technical validity of the prescription. Box I-1 presents a series of questions designed to aid in evaluating the technical considerations for compounding. The batch compounding of sterile preparations, especially in the hospital and home health care environments, has increased noticeably. There are a number of reasons for this increase, including the following:

- The changing patterns of drug therapy, such as home parenteral therapy and patient-controlled parenteral administration
- The use in hospitals of injectable drugs that are not commercially available to meet individual patient needs or the prescriber's clinical investigational protocols
- Cost containment, whereby a pharmacy batch produces drug products that are intended to be similar to commercially available products

Batch compounding can reduce the cost of a medication that must be taken over a long period or continuously for a chronic condition. This process allows a patient to store the preparation at home and reduce the number of pharmacy visits. Pharmacists who choose to perform batch compounding should be capable and willing to do it properly, particularly when sterile drug products are involved (see Box I-2).

Economic Considerations

Several economic considerations must be weighed when making the decision to compound prescriptions, including a pharmacist's compensation for the service and the effect of the service on health care costs. Both factors are equally important.

BOX I-1 Technical Considerations for Compounding a Prescription

The following are technical considerations for compounding a prescription:

- Is the preparation commercially available in the exact dosage form, strength, and packaging?
- Is the prescription rational concerning the ingredients, intended use, dose, and method of administration?
- Are the physical, chemical, and therapeutic properties of the individual ingredients consistent with the expected properties of the ordered preparation?
- Will this compounded preparation satisfy the intent of the prescribing physician and meet the needs of the patient?
- Is there an alternative (e.g., different dosage form, different route of administration) by which the patient will receive a benefit?
- Is there a bona fide prescriber–pharmacist–patient relationship?
- Can ingredient identity, quality, and purity be assured?
- Does the pharmacist have the training and expertise required to prepare the prescription?
- Are the proper equipment, supplies, and chemicals or drugs available?
- Is there a literature reference that might provide information on use, preparation, stability, administration, and storage of the compounded preparation?
- Can the pharmacist perform the necessary calculations to compound the preparation?
- Can the pharmacist project a reasonable and rational beyond-use date for the prescription?
- Is the pharmacist willing to complete the necessary documentation to compound the preparation?
- Can the pharmacist do some basic quality control to check the preparation before dispensing (e.g., capsule weight variation, pH, visual observations)?
- What procedures are in place for investigating and correcting failures?
- How long will the patient be using the preparation, and is the expected duration of therapy consistent with an appropriate expiration date? Alternatively, should the preparation be compounded in small quantities and dispensed to the patient at short intervals?
- Does the patient have the necessary storage facility, if required, to ensure the potency of the preparation until its beyond-use date?

Pharmaceutical compounding is a cognitive service; therefore, appropriate reimbursement is justified. The pricing of a compounded prescription should account for pharmacodynamic and pharmacotherapeutic decision making, formulation expertise, time involved, and reimbursement for materials. Compounding prescriptions can be attractive for a pharmacist both professionally and financially. Historically, compounding has been said to be an act whereby the professional and scientific knowledge of a pharmacist can find its expression. For those pharmacists dedicated to performing quality compounding, the professional, psychological, and financial rewards can be substantial.

Compounding prescriptions can be one way of lowering the cost of drug therapy. In some cases, a pharmacist's preparation of a specific prescription for a patient may be less

BOX I-2 Technical Considerations for Batch Compounding

The following are technical considerations for batch compounding:

- Will the processes, procedures, compounding environment, and equipment used to prepare this batch produce the expected qualities in the finished preparation?
- Will all the critical processes and procedures be carried out exactly as intended so that every batch produces the same high-quality preparation?
- Will the finished preparation have all the qualities as specified on completion and packaging of each batch?
- Will each batch retain all the qualities within the specified limits until the labeled expiration date?
- Will pharmacy personnel be able to monitor and trace the history of each batch, identify potential sources of problems, and institute appropriate corrective measures to minimize the likelihood of their occurrence?

expensive than a manufactured version, which may mean that the patient may actually obtain the drug rather than have to do without it. If compounding a prescription will enable a patient to afford the drug therapy, it must be considered.

Another way in which compounding may lower drug costs concerns the economic use of very expensive drug products that may have short shelf lives. If a patient does not need the entire contents of a vial or dosage unit, the remaining drug product is often discarded and wasted. In numerous instances, however, a pharmacist can divide the commercial product into smaller usage units, store it properly, and dispense the required quantity on individual prescriptions.

A related economic question involves the commercialization of compounded preparations. Over the years, many compounded preparations have eventually become commercially available. Table I-1 lists commercial products recently introduced to the market. Inevitably, a pharmaceutical manufacturer will produce a product when it becomes economically profitable to do so.

Summary

Compounding pharmacists are interested in and excited about their practice. In fact, many pharmacists intimately involved in pharmaceutical care have come to realize the importance of providing individualized patient care through the compounding of patient-specific preparations. As compounding pharmacy continues to grow, it will provide an opportunity for more pharmacists to use their innovative skills to solve patients' drug problems.

Pharmaceutical compounding provides pharmacists with a unique opportunity to practice their time-honored profession. It will become an even more important part of pharmacy practice in the future, particularly for those involved in community, hospital, long-term care, home health care, veterinary care, and specialty practices.

Although pharmacists should not hesitate to become involved in pharmacy compounding, they should be aware of the requirements for and uniqueness of formulating a specific drug product for a specific patient. This service is an important component in

TABLE I-1 Compounded Preparations That Are Now Commercially Manufactured

Aminopyridine (4-) capsules (fampridine)
Bevacizumab (Avastin—new packaging to Lucentis)
Buffered hypertonic saline solution
Buprenorphine nasal spray
Clindamycin topical solution
Colchicine injection
Colchicine tablets (Colcrys)
Dalfampridine (Ampyra) tablets
Dextromethorphan hydrobromide with quinidine sulfate capsules (Nuedexta)
Diazepam rectal gel (Diastat)
Erythromycin topical solution
Estradiol topical gel
Fentanyl lozenges
Fentanyl sublingual spray
Hydroxyprogesterone caproate injection (Makena)
Minoxidil topical solution
Nitroglycerin rectal ointment
Nystatin lozenges
Omeprazole and sodium bicarbonate liquid (Zegerid)
Premixed intravenous solutions (select ones)
Progesterone vaginal gel (Crinone)
Quinine sulfate capsules
Testosterone topical gel (Androgel)
Tetracaine–adrenalin–cocaine (TAC) solution

providing pharmaceutical care. After all, without the pharmaceutical product, there is no pharmaceutical care.

Reference

1. National Association of Boards of Pharmacy. Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy. Available at: www.nabp.net/publications/model-act. Accessed: September 22, 2015.

The new 4th edtion of The Art, Science, and Technology of Pharmaceutical Compounding presents in a logical and progressive format all the information that pharmacists and student pharmacists need to understand the purpose and processes of compounding. Author Loyd V. Allen Jr., the preeminent expert, covers basic guidelines, economic and technical factors that compounding pharmacists must consider, and all aspects of good manufacturing practices for compounded medications. Key Features: The initial chapters describe the requisite facilities and equipment, record keeping, calculations, and quali Find many great new & used options and get the best deals for The Art, Science, and Technology of Pharmaceutical Compounding by Loyd V. Allen (2016, Hardcover) at the best online prices at eBay! Free shipping for many products!Â Author Loyd V. Allen Jr., the preeminent expert, covers basic guidelines, economic and technical factors that compounding pharmacists must consider, and all aspects of good manufacturing practices for compounded medications. In this fifth edition, all chapters have been updated and several significantly revisedparticularly "Compounding with Hazardous Drugs"and three new chapters have been added: "Pharmaceutical Compounding Errors," "Foams," and "Compounding with Special Ingredients." by American Pharmacists Association. in The Art, Science, and Technology of Pharmaceutical Compounding, 5th Edition. The Art, Science, and Technology of Pharmaceutical Compounding, 5th Edition; doi:10.21019/9781582122632.appii. Publisher Website. Google Scholar. Appendix I: Drugs and Dosage Forms Not to Be Compounded (The FDA Negative List). Loyd V. Allen. Published: 1 January 2016. by American Pharmacists Association. in The Art, Science, and Technology of Pharmaceutical Compounding, 5th Edition. The Art, Science, and Technology of Pharmaceutical Compounding, 5th Edition; doi:10.21019/9781582 Loyd V. allen jr. . The Art, Science, and Technology of Pharmaceutical Compounding. , Washington, DC September 2003 Â· American journal of pharmaceutical education. Susan M. Jay. Read more.Â Join ResearchGate to discover and stay up-to-date with the latest research from leading experts in Art and Science and many other scientific topics. Join for free. ResearchGate iOS App.