Introduction to Compounding

INTRODUCTION

Webster's New World Dictionary defines the word compound as a verb meaning “1. to mix or combine, 2. to make by combining parts, and 3. to intensify by adding new elements.” Pharmaceutical compounding is the practice of extemporaneously preparing medications to meet the unique need of an individual patient according to the specific order of a prescriber. This differs from the traditional practice of pharmacy in that it involves a special relationship between patient, prescriber, and pharmacist.

After completing this chapter, you should be able to:

• Explain the purpose and reason for compounding prescriptions.
• Discuss the basic procedures involved in compounding.
• List the major dosage forms used in compounding.
• List and describe the equipment, supplies, and facilities required for compounding.
Overview of Compounding

Pharmacy is the only profession that allows the extemporaneous compounding of chemicals for therapeutic care. There has been an increase in the need for compounding prescriptions. Several reasons for this increase include the discontinuation of certain drugs by their manufacturer, the removal from the market of drugs by the Food and Drug Administration, and the unavailability of drugs in a strength or dosage form appropriate for a specific patient. Patients with sensitivities or allergies to preservatives or other certain excipients will need to have their medications compounded, leaving out the offending agent(s). A combination therapy that a prescriber desires, but that is not currently commercially available, can also be successfully compounded. These are just a few of the many scenarios that require the expertise of a compounding pharmacist.

The level of difficulty of preparing the compounded prescription is determined by the physical properties of the drug being prescribed and the dosage form desired either by the prescriber or the patient. In some cases compounding will be a simple two-step process, whereas in others it will require extensive knowledge and many steps to perform.

Regardless of the procedure, certain criteria must be considered for all compounded prescriptions. Research must be done on the active ingredient to determine cost effectiveness, availability, solubility, stability, and possible dosage forms. Every pharmacy that compounds prescriptions should have access to quality reference resources. Some of these valuable resources include the following books and journals:

- *Remington’s Pharmaceutical Sciences*
- *The Merck Manual*
- *The Merck Veterinary Manual*
- *Trissel’s Stability of Compounded Formulations*
- *Drug Facts and Comparisons*
- *United States Pharmacopeia*
- *Veterinary Drug Handbook* by Donald C. Plumb
- *International Journal of Compounding Pharmacists*
- Various Internet websites

Compounding a Prescription

In addition to researching the active ingredients and excipients needed in a compounded prescription, the preparer must also have knowledge regarding pharmaceutical calculations. This is one area of compounding where the potential for error is great. Something as simple as a misplaced decimal point can have devastating results for the patient. Only a properly trained individual should perform the critical calculations involved in formulating a compounded prescription, and no calculation or measurement should go unchecked by the pharmacist.

The first step in compounding a prescription is to obtain a formula or recipe that is prepared by a pharmacist, including all necessary ingredients.
and explicit instructions for the preparer. The source of the formula may be
one that has already been published or that has been created by the pharma-
cist in the compounding facility. If a formula is handwritten, it must be writ-
ten legibly, with instructions communicated clearly to the preparer. From the
formula or recipe, a worksheet should be created containing a list of active
ingredients and excipients and the exact amounts needed of each to prepare
the particular prescription. This worksheet should first be double-checked
for error and then referred to a checkpoint throughout the preparation of the
prescription. As each ingredient is weighed, it should be checked off the
worksheet. (This is especially necessary when a formula calls for multiple
active ingredients and excipients.) The weights of all active ingredients
should be confirmed by the pharmacist or (as individual state law allows) by
another pharmacy technician.

There is an extensive list of equipment used in pharmaceutical com-
pounding. When performing any task, you must be able to choose the ap-
propriate tool needed to prepare a quality product. It is important for you as
the compounding technician to be familiar with the available tools and their
functions.

**Equipment and Supplies**

Following is a partial list of compounding equipment and their basic functions:

- **balance**—for measuring ingredients
- **beakers**—for measuring ingredients and for mixing or heating
  ingredients
- **capsule filling equipment**—to prepare capsules
- **chopper/grinder**—to break up solids or ingredients of large particle size
- **electronic mortar and pestle**—for mixing creams and ointments and for
  reducing particle size
- **filter paper**—to remove particulate matter from a liquid
- **funnels**—to transfer liquids and powders
- **graduates**—for measuring liquids
- **heat gun**—to melt bases and to smooth the tops of troches or
  suppositories
- **homogenizer**—to reduce particle size and evenly suspend liquids
- **hotplates**—for melting bases
- **liquid blender**—for mixing liquids
- **magnetic stir plate**—for continuous stirring
- **magnetic stirrers**—for continuous stirring
- **molds**—to make troches and suppositories
- **mortars and pestles**—to mix powders and to reduce particle size
  glass—for liquids
  Wedgwood—for powders of significant particle size
  porcelain—for powders
ointment tile—for making creams and ointments
crème blender—to mix powders
refrigerator—for storage ingredients and prescriptions that need cold temperatures
safety glasses—to protect the preparer’s eyes from debris
sieves in various mesh sizes—to reduce particle size
spatulas—use for mixing creams and ointments and for retrieving chemicals from the bottle
spray bottles—to dispense cleaning solutions or distilled water
stirring rods—to stir liquids by hand
strainers—to remove particulate from a liquid
thermometers—to control temperature
tongs—to pick up items that should not be handled
tube crimper—to seal ointment tubes
tubes—to dispense creams and ointments
wash bottles—for washing
weigh boats/papers—to weigh ingredients on a balance
weights for calibration—to calibrate a balance

Compounding Facilities

An area suitable for compounding must be established before preparing a compounded prescription. The area should be separate from all other work areas and away from heavy traffic flow. The workspace should be large enough to accommodate all the necessary supplies. It should be clean and free of any clutter. Any object not directly involved in preparing the compound should be removed. All tools and surface areas should be cleaned just prior to use and again when the compound is complete. This can be accomplished by wiping everything down with isopropyl alcohol 70 percent or another suitable cleaning solution. This will safeguard the compounded prescription from possible cross-contamination as well as prevent microbial growth within the final product.

When mixing the active ingredient(s) with the excipient(s), the principle of geometric dilution should be practiced. This is to start with the ingredient of the smallest amount and double the portion by adding the additional ingredients in order of quantity. Each addition should result in a “doubled” amount until all the ingredients are mixed in. This process ensures even distribution of the active ingredient throughout the final product.

Determining the most appropriate dosage form will depend not only on the drug that is being compounded, but on the patient as well. The patient is probably the most important factor to consider when deciding which dosage form to prepare for a compounded prescription. Some common dosage forms that can be effectively compounded are capsules, liquids, transdermal gels, creams, ointments, suppositories, and chewables. Each form will require precise instructions for preparing a quality, efficacious product. (See Figure 9-1.)
Dosage Forms and Basic Guidelines

There are many types of dosage forms. They include capsules, liquids, solutions, suspensions, emulsions, ointments, suppositories, creams, transdermal gels, and otic and nasal preparations. A discussion of each follows.

CAPSULES

Capsules, as an oral dosage form, have been used for more than a century. The capsule has an important role in drug delivery in that it is extremely versatile and offers a broad range of dosage options for patients. The capsule offers flexibility in dosing to the prescriber as well as to the patient with specific needs.

Capsules can be prepared either by hand or by using a capsule machine. Which method is used will depend on the quantity needed and the physical characteristics of the powders included in the formula.

Using a capsule machine saves time and produces a number of capsules at a time, depending on the size of the machine and the desired quantity. Simply blocking off some of the holes can make a smaller number of capsules.

LIQUIDS

A liquid will be either in the form of a solution or a suspension. A solution is a liquid containing one or more active ingredients that are completely dissolved. A suspension is a liquid containing one or more active ingredients that remain solid and are dispersed evenly throughout the liquid upon being shaken. Solubility is usually the determining factor in the decision of which type of liquid to make.
SOLUTIONS
In an aqueous solution, the water-soluble chemical is dissolved in the water phase of the compound. This may consist of just enough distilled or preserved water to dissolve the drug, or the water may be as much as 50 percent of the final volume. After the drug is completely dissolved in the water, adding flavoring agents and bringing it to the final volume with a sweetening agent such as Ora-Sweet, Simple Syrup, or Karo Syrup may complete the compound. Although the drug is in solution, it may be necessary to shake the liquid before use in order to evenly distribute the flavor.

SUSPENSIONS
A suspension is a liquid preparation that contains insoluble solid particles uniformly dispersed throughout the vehicle. A suspension needs to be shaken prior to administration to ensure the proper dose is dispersed. If a drug is to be suspended, a suspending agent such as Ora-Plus or Karo Syrup will be needed.

EMULSIONS
An emulsion is another type of liquid or semi-solid preparation that can be taken orally or applied topically. Emulsions are prepared whenever two immiscible liquids must be dispensed in the same preparation. An emulsifying agent is used to hold the two together. One part is oil and the other part is aqueous. Emulsions are either water in oil (w/o) or oil in water (o/w), depending on the external phase of the final product. Generally, emulsions that are to be used internally are of the o/w type, whereas emulsions for topical use can be of either type.

Emulsions should be shaken well before use in order to temporarily suspend the aqueous phase into the oil phase and equally distribute the active ingredient(s).

OINTMENTS
An ointment is a semisolid preparation that is usually applied to the skin or to mucosal tissue. An ointment does not penetrate into the skin, but rather stays on top of the skin. Ointments should be soft and easily spread. They should also be smooth in texture, not gritty. Common ointment bases used in compounding include white petrolatum, hydrophilic petrolatum, Aquaphor, hydrous Lanolin, and PEG ointments.

To ensure a smooth ointment, the particle size of a powder being incorporated into the base should be reduced to an impalpable form by comminuting. This can be achieved by using a Wedgwood or porcelain mortar and pestle or by forcing the powder(s) through a size 100 mesh sieve. Once the particle size is reduced, the powder can then be mixed into the base, using geometric dilution. At times it will be necessary to “wet” the powder with a solvent such as glycerin, ethoxydiglycol, or propylene glycol before incorporating them into the base. Other times the drug will be dissolved in oil, such as mineral oil, prior to mixing with the base.
CREAMS

A cream is a soft solid that is opaque and usually applied externally. Creams dissipate into the skin, healing the affected area from the inner layers of the dermis.

Medications are usually suspended or dissolved in a water-soluble base when compounding a cream. A cream must be smooth, and the active ingredients should be dissolved completely in order for them to be totally absorbed into the skin. Cream bases that are available for compounding include vanishing cream base and HRT base, as well as some commercially prepared creams such as Cetaphil, Eucerin, and Lubriderm.

When adding active ingredients to creams, it is critical to practice the principles of geometric dilution to ensure even dispersion. A wetting agent may be necessary; and, again, the volume required to wet the powder should be calculated into the formula when determining the amount of base needed to bring the product to the final desired quantity.

SUPPOSITORYES

A suppository is a solid dosage form that is inserted into the rectum or vagina. The suppository melts and softens or dissolves at body temperature, thus allowing absorption of the medication into the surrounding tissues. Suppositories can either have a systemic effect or a local effect depending on the desired effect expected by the prescriber or on the drug being used. Suppositories can be made in several different shapes and sizes, depending on the patient and the disease state being treated.

When determining which base is most appropriate to use in compounding suppositories, you will have to consider the physical characteristics of the drug ordered as well as the patient. Some of the common bases used for preparing suppositories include fattibase, polybase, and cocoa butter. A drug may either be dissolved in the base or it may need to be suspended, depending on the physical characteristics of the drug being ordered. Whether the drug is dissolved or suspended, the active ingredients and excipients should be added in geometric proportion to ensure that the active ingredient is equally dispersed throughout.

TRANSDERMAL GELS

The transdermal gel is a unique, semisolid dosage form that is becoming increasingly popular. Transdermal gels have special absorption enhancers that "push" the medication through the layers of the skin so that the medication can be absorbed into the bloodstream. The transdermal gel is an especially desirable alternative for pediatric patients, animals that are difficult to "pill" or otherwise medicate, the elderly, and patients who are physically or mentally disabled.

The most common form of compounded transdermal gel therapy is a two-phase vehicle made from pluronic lecithin organogel. It consists of both an oil phase and an aqueous phase, making it a suitable choice for many chemicals. The oil phase, which is lecithin isopropyl palmitate, is generally in a concentration of 22 percent, and the balance is made of poloxamer. Oil soluble drugs should be dissolved in the oil phase, whereas water-soluble drugs should be
dissolved in the aqueous phase. The determined amount of drug is dissolved in the appropriate phase, and then the two components are mixed together by using a shearing action. This shear force is necessary for proper micelle formation in the gel. The poloxamer gel is a liquid, which is stored in the refrigerator. When brought to room temperature, it will form a gel. It is important for the final product to be stored at room temperature. Auxiliary labels to this effect (as well as other instructions for the patient, not included on the prescription label) should be placed on the package prior to dispensing.

**OTIC**

Preparations for the ear are either in a liquid, a powder, or an ointment. Solutions and suspensions are instilled into the ear, whereas ointments are applied to the external ear. Powders are used infrequently, but would usually be administered to the ear canal by a physician. Otic preparations are generally used to treat local infections and the pain associated with them. Other otic products are used to dissolve or remove blockages that can lead to infection.

The vehicles most often used when compounding otic liquids are propylene glycol, glycerin, polyethylene glycol, vegetable oil (especially olive oil), and, occasionally, mineral oil. It is necessary to use a viscous liquid such as one of these, since it will adhere to the ear canal. Water and alcohol may be used as a vehicle, but are typically used as solvents for the drugs being compounded or used in an irrigating solution. The physical characteristics of the ingredients used in compounding otic preparations that need to be considered include solubility, viscosity, and tonicity. Almost always, a preservative will be used when preparing an otic preparation. Although otic preparations need not be sterile, it is important for the pharmacy technician to follow quality control procedures for preventing cross contamination or microbial growth in the compound. Many chemicals used in otic preparations are soluble in the vehicles used in compounding them. Due to the general viscosity of these products, a suspending agent is usually not necessary if the drug is insoluble.

When compounding a liquid for otic use, the drug and any preservatives or other excipients are accurately weighed and then dissolved or mixed with approximately three-quarters of the vehicle. When the drug is completely dissolved or evenly suspended, the preparation is then brought to final volume with more of the vehicle. When an ointment is being prepared, the drug and any other ingredients are accurately weighed and then mixed into the base by using the principles of geometric dilution.

**NASAL**

Preparations for nasal administration are in the form of solutions, suspensions, gels, or ointments. These preparations may be used locally or systemically, depending on the nature of the drug and the vehicle it is in.

In addition to the active ingredient, several excipients will most likely be used. These include the vehicle, buffers, preservatives, and tonicity-adjusting agents. Since nasal preparations are generally dispensed in multiuse containers,
it is necessary to use a preservative. The pH must be adjusted so that maximum stability is obtained. Two common vehicles used for nasal solutions are sodium chloride 0.9 percent and sterile water for injection.

Ingredients for nasal preparations should be sterile, and aseptic technique should be used to make them. Sterility may be obtained by filtration or autoclaving. If a drug is water soluble, it will be dissolved in a portion of the vehicle and the liquid will be brought to final volume with the vehicle. A suspension will require that the active ingredient and any excipients be mixed by using geometric dilution with a suspending agent and then brought to final volume with the appropriate vehicle. Mixing the active ingredient and any excipients with the base by using the principles of geometric dilution makes nasal gels or ointments.

Quality control procedures should be observed when making nasal preparations. Prior to dispensing, the pharmacist should determine clarity, pH, and correct volume or weight.

VETERINARY COMPOUNDING

Veterinary compounding is one of the fastest growing areas of pharmaceutical compounding. Medication doses are usually calculated on the basis of milligrams per kilogram. Because of the vast difference in the size and physiology of animals, this makes appropriate dosing nearly impossible when using manufactured products.

The same principles used in human compounding of medications apply to veterinary compounding. Stability, solubility, drug availability, dosage form choices, cost effectiveness of drug sources, and quality of final product are all factors to be considered before attempting to compound for animals.

In addition to capsules, flavored liquids, transdermal gels, and suppositories, the chewable treat is another dosage form available for pharmaceutical compounding. A chewable form made from a base of ground food product and gelatin mixed with the active ingredient is an excellent choice for animals. Some flavor choices for these chewable forms include liver, tuna, salmon, shrimp, chicken, and beef. Again, solubility is taken into consideration when preparing the treat form. If a drug is water-soluble it can be incorporated into the gelatin phase of the compound. If insoluble it will be mixed in geometric proportion with the solid, or food, phase of the compound and then mixed with the gelatin. The mixture is then forced by way of a syringe or other means into precalibrated molds. The final product is a soft chewable form that can be offered to the animal as a treat, or mixed in with a small amount of the animal’s favorite food, for consumption.

CONCLUSION

Extemporaneous compounding is a special service provided by a number of community-based pharmacies. Additional training, skills, and practice are required for a pharmacy technician to assist in compounding, but compounding also provides a number of advanced professional opportunities for those who pursue these skills.
CHAPTER REVIEW QUESTIONS

1. What are some of the factors that must be considered before compounding a prescription medication?
   a. cost effectiveness, availability, solubility, and stability
   b. suspending agent, profit margin, and ease of preparation
   c. proper tools, adequate support personnel, and time
   d. insurance reimbursement, available flavoring agents, active ingredient, and source

2. The extemporaneous compounding of prescription medications differs from traditional pharmacy in that it involves a relationship between:
   a. mother, father, and child
   b. patient, practitioner, and pharmacist
   c. pharmacist, patient, and insurance carrier
   d. doctor, nurse, and patient

3. Pharmacy is the only profession that allows the extemporaneous compounding of chemicals for:
   a. resale
   b. veterinarians
   c. therapeutic care
   d. use in physician’s offices

4. Of the following reference materials, which would not be necessary in a compounding facility?
   a. Remington’s Pharmaceutical Sciences
   b. The Merck Manual
   c. Drug Facts and Comparisons
   d. Pharmacy Times Magazine

5. Which area of the compounding procedure has the greatest potential for error?
   a. pharmaceutical calculations
   b. retrieving the proper chemical
   c. selecting the proper vehicle
   d. choosing the best flavor

6. Who is responsible for checking the calculations performed for a specific formula?
   a. another technician
   b. the pharmacist
   c. the person who performs the calculations
   d. ancillary personnel

7. The compilation of ingredients and instructions is known as the:
   a. worksheet
   b. menu
   c. formula
   d. list

8. In order to avoid cross-contamination, the compounding area should be cleaned:
   a. before the procedure
   b. after the procedure
   c. daily
   d. both before and after the procedure

9. Transdermal gels in the form of a pluronic lecithin organogel are considered to be:
   a. an emulsion
   b. an ointment
   c. a cream
   d. a suspension

10. Which of the following types of mortar and pestle would be the ideal choice when working with liquids?
    a. porcelain
    b. glass
    c. Wedgwood
    d. any of the above
Resources and References


