

Pharmacy Technician Program

Chapter 8: Principle of Compounding

Coursework 101





Principle of Compounding

This chapter provides an overview of extemporaneous compounding, preparation of solutions, and record-keeping of procedures.



Introduction to Compounding

A. Compounding in the Pharmacy

1. **Compounding as it relates to pharmacy; includes the preparation, mixing, assembling, packaging or labeling of a drug in response to a prescription written by a licensed practitioner.**
2. **Today, most dosage forms of medications are already prepackaged by the manufacturer and thus the Pharmacist's role is more in the redistribution of medications and the clinical aspect of Pharmaceutical Care.**



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3. **Extemporaneous Compounding** is defined as the timely preparation of a drug product according to a physician's prescription, a drug formula, or a recipe in which calculated amounts of ingredients are made into a homogenous (uniform) mixture.
 - a. Pharmacy Technicians are also doing extemporaneous compounding of medications.
 - b. Extemporaneous compounding should be documented on a master formula sheet.



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- c. Extemporaneous compounding is done when:
- i. certain medical needs of individual patients cannot be met by the use of an approved commercial drug product,
 - ii. to make a dose form not manufactured by a pharmaceutical company,
 - iii. the dilution of adult dose of meds to pediatric/geriatric strengths,
 - iv. the conversion of solid dosage forms to solutions or suspensions,



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- v. the combination of topical dermatological products not available by the manufacturer, and
- vi. when inactive ingredients of commercial products may cause allergic reactions in individuals and need to be removed.
- vii. “Good Manufacturing Practices” are the guidelines that pharmacists and manufacturers must follow to guarantee that a product is (extemporaneously) compounded appropriately.



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B. Compounding and USP 797 Guidelines

1. According the USP 797

(<http://www.usp.org/audiences/pharmacist/797FAQs.html#Q5>) (Personal Cleansing and Garbing: Questions 53-71)

requires that all individuals who enter the buffer area or clean room shall be fully garbed with appropriate protective equipment.

- a. Remove outer garments and jewelry (including piercings above the neck)
- b. Garb order from dirtiest to cleanest
- c. Don shoe covers, hair covers, face masks, and beard covers.



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- d. Perform hand/arm hygiene**
 - i. USP Chapter <797> harmonized with CDC Guidelines for Hand Hygiene**
 - ii. Hand washing is defined as the vigorous, brief (30 seconds) rubbing together of all surfaces of lathered hands, followed by rinsing under a stream of water.**
 - iii. Hand washing suspends microorganisms and mechanically removes them by rinsing with water. The fundamental principle of hand washing is removal, not killing.**
 - iv. Single most important way to reduce the risks of transmitting germs.**
 - v. no nail polish**



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- e. Don disposable (non sterile) gowns
- f. Don gloves (sterile)



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2. Inside the clean area

- a. Inside the clean area, cleanse hands and arms with alcohol-based surgical hand scrub with persistent activity.
- b. After hands and arms are dry, don sterile powder-free gloves compatible with sterile 70% IPA
- c. Repeatedly apply sterile 70% IPA to contact areas of gloves whenever non sterile surfaces are touched (e.g. vials, counter tops, carts)



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- d. if a glove is torn during compounding it is not necessary to do a hand cleansing with soap and water within 30 seconds, but the hands should be re-sanitized using the alcohol-base (waterless) surgical hand antiseptic agent.**
 - i. All of the cleansing, garbing and gloving requirements also apply to compounding in CAIs and CACIs.**
 - ii. Exception: If the manufacturer of the CAI or CACI provides written documentation of statistically validated testing supporting any garbing component(s) that are not required.**



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C. Compounding Equipment

1. Balances-Class III Prescription Balance also known as Triple Beam Balance which has a left and right pan.
 - a. You place the substance to be weighed in the left pan and the weights on the right pan.
 - b. This scale should be kept in an area to avoid high traffic.
2. Forceps or Tweezers...the tool used to transfer weights.



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3. Spatulas...used to transfer solid materials to the weighing pans.

- a. The type of spatula to use is dependent on what is being transferred or mixed
 - i. available in stainless steel, plastic and hard rubber,
- b. used to transfer powders, ointments, and creams to weighing pans
- c. used to mix ingredients together into homogenous mixtures



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4. The Ointment slab provides a clean, hard surface for the mixing of compounds.
 - a. Most ointment slabs are ground glass plates, that provide a non-absorbable surface area.
5. For multiple compounding, many pharmacies purchase Parchment Papers that serve to provide a non-absorbable surface area when placed over an ointment slab; but are easily disposed of after use without the necessary cleaning involved between mixtures.



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6. Mortar (bowl) and Pestle which is used to grind or mix ingredients in a mortar.
 - a. The incorporation of a liquid (levigation) can further reduce particle size.
 - b. They are available in glass, porcelain, Wedgewood or marble.
 - i. Glass is preferable for mixing liquids and semi-soft dosage forms.



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7. Graduates are used in the measurement of liquids.
 - a. Most graduates are marked “TD” which means, “to deliver”.
 - i. This marking indicates that the measurement of this graduate will compensate for the excess liquid that adheres to the surface of the graduate after emptying.
 - b. Conical graduates have a wide mouth and a wide base to allow for the stirring of liquids with a glass stirring rod.
 - i. As the diameter of the graduate increases, the accuracy decreases.
 - ii. The conical graduate varies in size from 10mL to 4000mL.



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c. Cylindrical graduates are uniform from top to bottom and are the most accurate graduate for the measurement of liquids.



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8. Pipettes...long, thin, calibrated glass tube for measuring liquid volumes less than 1.5 ml.



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D. Technique for Measuring Liquid Volumes

1. Reading must be done at eye level



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2. The correct reading is the mark at the bottom of the meniscus
 - a. The meniscus is moon-shaped or slightly concave and bowed inward toward center
 - b. Measure by placing the eyes at the level of the liquid.
 - c. Read the level of the liquid at the bottom of the meniscus.
 - i. Note: The volume of fluid measured in a conical (cone shaped) graduate is still at the bottom of the meniscus.



Terms related to the Comminution and Blending of Drugs

A. Common Terms

1. **Comminution** is the act of reducing a substance to small fine particles.
2. Blending is the act of combining two substances.
3. **Trituration** is the process of rubbing, grinding or pulverizing a substance to create fine particles. Usually done with a mortar and pestle using a rapid motion with minimal pressure.



Terms related to the Comminution and Blending of Drugs

4. **Levigation is mixing a powder with a vehicle in which it is insoluble to produce a smooth dispersion of the drug. The dispersion is then mixed with the base.**
 - a. Mineral oil is a good levigating agent for an ointment.
5. **Pulverization by intervention is the process of reducing the size of particles in a solid using the aid of an additional material in which that material is soluble - a volatile solvent that evaporates.**
 - a. Camphor, alcohol, iodine, and ether are all possible solvents.



Terms related to the Comminution and Blending of Drugs

6. **Spatulation is the process of combining substances by means of a spatula.**
7. **Sifting is used to combine powders.** Powders can also be combined by tumbling, which involves placing the powders into a bag and shaking it.



Geometric Dilution

A. Homogenous mixture

1. Geometric Dilution is the process by which a homogenous mixture or even distribution of two or more substances is achieved.
 - a. When using this method, the smallest quantity of active ingredient is mixed thoroughly with an equal volume of the diluent or base on the ointment slab.
 - b. More diluent (base) is added in amounts equal to the volume of the mixture on the ointment slab.
 - c. This process is repeated until all the diluent is incorporated in the mixture.



Geometric Dilution

2. When geometric dilution is not used it may result in gritty and scattered powder that fails to blend in the ointment/cream base being used.
 - a. A non-homogenous mixture can not only pharmacologically affect the therapeutic effect, but can also cause serious topical skin reactions.
3. You've been told that 100% Accuracy is your goal and that remains true. However, it is generally agreed that pharmaceutical products should be prepared with a low percentage of error. The Official Compendium allows a tolerance of plus or minus 5 percent for most formulas. The term "tolerance" implies that there is a consequence for making errors.



Preparation of Liquids, Solids in Liquids and Ointments/Creams

A. Liquids

1. Liquids such as Solutions and Suspensions, are the most common form of compounded medications.
2. A solution is a clear liquid in where the drug is completely dissolved.



Preparation of Liquids, Solids in Liquids and Ointments/Creams

3. A suspension is a liquid preparation that contains fine drug particles that are distributed uniformly throughout the solution.
 - a. Suspending Agents are a thickening agent that gives some structure to a suspension. Allows easy dispersion of particles.
 - i. Example: Carboxymethylcellulose, Tragacanth
 - ii. The reconstitution of an antibiotic such as Amoxicillin would be an example of a suspension.
 - b. Suspensions always require shaking before use (“Shake Well” auxiliary label)



Preparation of Liquids, Solids in Liquids and Ointments/Creams

B. Solids in Liquids

1. When solids are required in a solution, it is important to reduce the particle size of the solid by using the mortar and pestle (trituration).
 - a. In some cases, the incorporation of other agents are needed to ensure finer particle size and in the case of suspensions, to ensure even distribution of particles.
2. A dilute solution contains a very small amount of particles or solute in solution.



Preparation of Liquids, Solids in Liquids and Ointments/Creams

3. A concentrated solution contains large quantities of solute in solution and a saturated solution contains the maximum amount of solute that can be dissolved in a solvent or at a given temperature or pressure.



Preparation of Liquids, Solids in Liquids and Ointments/Creams

C. Ointments/Creams

- 1. Ointments and Creams are semisolid dosage forms used externally.**
- 2. They are often used when the prescribing physician requires the combination of two or more ointments or creams in a specified ratio or the incorporation of a drug into an ointment or cream base.**



Preparation of Liquids, Solids in Liquids and Ointments/Creams

- 3. Ointments are characteristically oil based, while creams are water based.**
- 4. Since the direct mixing of ingredients is not always workable, the incorporation of other agents such as a wetting agent (displaces air from particles and allows them to mix better, e.g. Alcohol) or a levigation agent (reduces particle size, e.g. Mineral Oil, Glycerin) is needed to ensure finer particle size.**



Preparation of Liquids, Solids in Liquids and Ointments/Creams

D. Preparation of Suppositories

1. One or more active ingredients are placed into a base (cocoa butter, hydrogenated vegetable oil, glycerinated gelatin).
2. Once the base is melted, add active ingredients.
3. Pour liquid into the mold and chill, immediately.



Preparation of Liquids, Solids in Liquids and Ointments/Creams

E. Preparation of Capsules

1. Hard gelatin capsules have two parts:
 - a. The body is the longer and narrower part, and the cap is shorter and fits over the body.
2. A “punch” method is usually used to fill the capsules.

Powder placed on a clean surface and formed into a cake approximately $\frac{1}{4}$ to $\frac{1}{3}$ the height of the capsule body.



Preparation of Liquids, Solids in Liquids and Ointments/Creams

3. The body is punched into the cake repeatedly until the capsule is full.
4. Cap is placed snugly over the body.
5. Capsule is weighed to verify the dosage.



Labeling, Record Keeping and Cleanup

A. Procedure

1. Products must be labeled with Rx label.
 - a. Ingredients of a compound and the amounts, by volume, should be stated on the label, as well as the date the product was compounded.
2. **A record of compounding should be kept.**
 - a. The compounding record includes a record of the compounding, including ingredients, amounts of ingredients, preparer's name, and name of supervising pharmacist.



Labeling, Record Keeping and Cleanup

- b. The record should provide all the information someone would need to recreate the compounded product plus information on the products used in case of a recall.



Calculations

A. Compounding Calculations

Two of the most crucial steps in compounding any pharmaceutical product are the accurate calculation and measurement of the component ingredients of the formulation.

In order to carry out these critical functions, the Pharmacy Technician must have a working knowledge of the metric system, ratio & proportion and percentages. With these skills, the Pharmacy Technician should be able to solve almost all extemporaneous compounding calculations accurately.



Calculations

You will find most solutions/suspensions marked as a specific concentration or strength of active drug per volume of liquid. In some cases, you may find solutions marked in a percentage strength and in most cases, ointments/creams marked as a percentage of active ingredient.

Percentage (%) means “by the hundred” or “in a hundred.” A percent is actually a fraction, but a fraction with a specific denominator. The denominator is always 100. In the case of liquids, the percentage is mL per 100 mL . In the case of ointments/creams, the percentage is g per 100 g.