Tech Lectures®

For the Pharmacy Technician

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Section XXIV - Principles of Compounding

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Principles of Compounding

Introduction

Goals & Objectives

The Pharmacy Technician will have a basic understanding of the following:

1. Compounding defined
2. Reasons for compounding
3. Compounding equipment
4. Principles of compounding
5. Calculations involved

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. *Extemporaneous* compounding is defined as the timely preparation of a drug product according to a physicians prescription, a drug formula, or a recipe in which calculated amounts of ingredients are made into a homogenous (uniform) mixture. *Extemporaneous* compounding is done when certain medical needs of individual patients cannot be met by the use of an approved commercial drug product.

Today, most dosage forms of medications are already pre-packaged by the manufacturer and thus the Pharmacist role is more in the redistribution of medications and the clinical aspect of Pharmaceutical Care. The role of the Pharmacy Technician continues to grow as Technicians are taking on more of the dispensing functions once reserved for the Pharmacist alone. Pharmacy Technicians are also doing extemporaneous compounding of medications.

Reasons for Extemporaneous Compounding Today

a. Unavailable dosages, strengths and routes of commercial products

b. Dilution of adult doses of medications to Pediatric/Geriatric strengths

c. Conversion of solid dosage forms to solutions or suspensions

d. Combination of topical dermatological products not available by the manufacturer

e. Inactive ingredients of commercial products which may cause allergic reactions in individuals.

Equipment

Balances

Class A Prescription Balance

The Class A Prescription Balance is a two-pan torsion type balance that utilizes both internal and external weights. The Class A Prescription Balance is used in the Pharmacy setting as a means of determining the weight of a material to be used in the compounding of a prescription or manufacturing of a dosage form. This balance is currently required in all pharmacy settings and must meet the requirements of the National Bureau of Standards (NBS).

The minimum weight that can be weighed on this balance is 120 milligrams (mg) and the maximum weight is 120 grams (gms). The Class A prescription balance has a sensitivity of 6 mg that means just 6 mg of a substance will move the pointer of the balance one division off equilibrium or one degree.

Class A Prescription Balance Weighing Procedure

1. With the balance locked, place a weighing paper on each pan. Place the desired weight on the **RIGHT** pan; place the material to be weighed on the **LEFT** pan
2. Release the lock of the balance and observe the position of the indicator
3. Lock the beam and adjust the amount of material
4. A swinging balance is the most accurate method of measuring. This is indicated when the pointer swings an equal number of divisions to both sides of the central position
5. The final measurement should be determined with the cover down
6. To avoid mistakes in totaling the weights, they should be totaled three times
    a. as they are placed on the pan
    b. from the vacant positions in the weight box
    c. and as they rest on the pan

Proper care of the Class A Prescription Balance is important to ensure accurate measurements. Always keep the balance in the locked position, except when equilibrium is being tested and never add or remove weight or materials unless the balance is in the locked position. The balance should be kept clean at all times, and care should be taken to avoid vibration, dust, moisture and corrosive vapors. The balance cover should be kept down at all times except when the balance is in use.

Bulk Balance

The Bulk Balance or Counter Balance is less accurate than the Class A Prescription Balance and is primarily used to weigh large quantities of material. It has a limit of 5 Kilograms (Kg) and a sensitivity of 100 mg.

Analytical Balance

With the advent of new technology, the Analytical Balance is finding its way from Pharmaceutical analytical laboratories into the Pharmacy setting. Due to convenience, precision and accuracy, as well as a sensitivity of a digital readout of 0.1 mg, most pharmacies prefer the use of this balance.

Weights

Weights used for the Class A Prescription Balance and other balances are made of brass or polished metal and must be maintained and handled properly. These sets usually contain cylindrical weights ranging from 1 to 50 gms and fractional weights of 10 to 500 mg. Once yearly the weights should be calibrated to ensure accuracy.

Care of Weights

a. weights should never be touched by the hand

- body oils will increase their weight and accelerate the corrosion of the weights
- should manipulate with plastic or plastic tipped tweezers to prevent oxidation of metal

b. weights must be stored in clean state

- in a special rigid and compartmentalized covered box

c. weights cannot be dropped or dented

Spatula

Spatulas are used to transfer solid ingredients such as powders, ointments, creams to weighing pans. They are also used to mix ingredients together into homogenous mixtures. Spatulas are available in stainless steel, plastic and hard rubber, the type of spatula to use is dependent on what is being transferred or mixed.

Mortar and Pestle

The mortar and pestle is used to grind particles into fine powders (trituration). The incorporation of a liquid (levigation) can further reduce particle size. Mortar and Pestles are made of Glass, Porcelain, Wedgwood or Marble. Glass is preferable for mixing liquids and semi-soft dosage forms.

Graduates

Graduates are used in the measurement of liquids. Most graduates are marked "TD" which means, "to deliver". 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.

Conical Graduate

The Conical graduate has a wide mouth and wide base to allow the stirring of liquids with a glass stirring rod. As the diameter of the graduate increases, the accuracy decreases. The conical graduate varies in size from 10ml to 4000ml.

Cylindrical Graduates

The Cylindrical graduate is uniform from top to bottom and is the most accurate graduate for the measurement of liquids.

Graduate measuring

- reading must be done at eye level
- correct reading is the mark at the bottom of the meniscus

  meniscus: surface of the liquid that bulges downward

Ointment Slabs

Along with the mortar, pestle and spatula, the Ointment Slab is mainstay in the Pharmacy setting. Ointment slabs provide a clean, hard surface for the mixing of compounds. Most ointment slabs are ground glass plates, that provide a non-absorbable surface area. For multiple compounding, many pharmacies purchase Parchment Papers that serve the same purpose when placed over an ointment slab, but are easily disposed of after use without the necessary cleaning involved between mixtures.

Principles of Compounding

Liquids

Liquids such as Solutions and Suspensions, are the most common form of compounded medications. A solution is a clear liquid in where the drug is completely dissolved. A suspension is a liquid preparation that contains fine drug particles that are distributed uniformly throughout the solution. The reconstitution of an antibiotic such as Amoxicillin would be an example of a suspension. Suspensions always require shaking before use.

Solids in Liquids

When solids are required in solution, it is important to reduce the particle size of the solid by using the mortar and pestle (trituation). 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.

A *dilute solution* contains a very small amount of particles or solute in solution. 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.

Ointments / Creams

Ointments and Creams are semisolid dosage forms used for externally. The 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. Ointments are characteristically oil based, while creams are water based.

Because the direct mixing of ingredients is not always workable, the incorporation of other agents such as a wetting agent or levigating agent is needed to ensure finer particle size.

Wetting Agents: displaces air from particles and allows them to mix better

Example: Alcohol

Levigating Agents: reduces particle size

Example: Mineral Oil, Glycerin

Suspending Agents: a thickening agent that gives some structure to a suspension. Allows easy dispersion of particles.

Example: Carboxymethylcellulose, Tragacanth

Geometric Dilution

Extemporaneous compounding of ointments and creams oftentimes involves the use of the mortar & pestle, spatula and the ointment slab. The key to a homogenous mixture is to use these tools properly and to incorporate the method of *Geometric Dilution* in the preparation of all ointment / cream products.

Geometric Dilution is the process by which a homogenous mixture or even distribution of two or more substances is achieved. 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. More diluent (base) is added in amounts equal to the volume of the mixture on the ointment slab. This process is repeated until all of the diluent (base) is incorporated in the mixture. This method, though time consuming, will create a homogenous mixture or smooth dispersion of the drug in the ointment/cream base.

In some cases, due to time constraints or lack of experience, *Geometric Dilution* is not used in the Pharmacy setting and mixtures are just mixed together haphazardly. This "*slap them together mixture*" may result in gritty and scattered powder that fails to blend in the ointment/cream base being used. A non-homogenous mixture can not only pharmacologically affect the therapeutic effect, but can also cause serious topical skin reactions.

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.

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.

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 mls per 100 mls. In the case of ointments/creams, the percentage is gms per 100 gms.

Example I:

Zinc Oxide Ointment is used as a skin protectant on small areas of exposure by scattering UV light and preventing adsorption. In the following formula you are compounding, how much Zinc Oxide is needed to make 240 grams?

Zinc Oxide Ointment

Al Hydroxide	5 %
Zinc Oxide Powder	12 %
Aquaphor (qsad)	240 gms

In this formulation you would notice that Zinc Oxide (ZnO) Powder is 12% or 12 grams per 100 grams of ointment base and the total volume required is 240 grams. Using this information, you would set up the following proportion and solve for *x*:

Have = Want

$$\frac{12 \text{ grams ZnO}}{100 \text{ grams Base}} = \frac{x \text{ grams ZnO}}{240 \text{ grams Base}}$$

x = 28.8 grams of ZnO is needed

If you were to calculate the Al Hydroxide in this formula using he same method, you would come up with 12 grams of Al Hydroxide is needed.

In this formulation you would be triturating 28.8 grams of Zinc Oxide and 12 grams of Al Hydroxide in the mortar & pestle to further reduce the particle size. If necessary you can use a small amount of levigating agent such as Mineral Oil, to reduce the particle sizes even smaller.

Then to ensure a homogenous and well-defined mixture, it is important that you use geometric dilution when mixing all of the ingredients together on an ointment slab.

Example II:

Boric Acid is used either as an antiseptic or in the ointment formulation as a counterirritant. How would you make a 60 ml solution containing 1 gram Boric Acid using a stock bottle containing 5% boric acid?

Realize that 5% of boric acid means 5 grams boric acid per 100 ml solution. To figure out how much of this solution to use you would set up the following ratio & proportion and solve for x:

$$\frac{5 \text{ grams}}{100 \text{ ml}} = \frac{1 \text{ gram}}{x \text{ ml}}$$

$$x = 20 \text{ ml}$$

You will need 20 ml of 5% Boric Acid solution . Since your total volume is to be 60ml, you will need to add 40 ml of deionized or distilled water to achieve a total volume of 60 ml. In this case you would use a Cylindrical Graduate for measurement to ensure accuracy.

Conclusion

Although extemporaneous compounding is not used often in the average Pharmacy setting, some pharmacies specialize in compounding and Pharmacy Technicians prepare these compounds. Much hands-on experience is needed to ensure a product is not only calculated correctly, but also prepared correctly. Other avenues of compounding include tablet/capsule formulations, suppositories, Intravenous solutions, and in some Pharmacy settings, medicated candy suckers. With proper training and guidance and final check by a Pharmacist, there is no reason why a Pharmacy Technician cannot become an expert in extemporaneous compounding.

About the Author

Joe Medina, CPhT, BS Pharmacy, former Program Director of a Pharmacy Technician Program at two community colleges in Colorado is a lifetime national advocate for the Pharmacy Technician Profession. Mr. Medina has helped produce several textbooks and co-authored *the* "*Pharmacy Technician Workbook & Certification Review*" through Morton Publishing. With fifteen years as a Pharmacy Technician and twelve years as a Pharmacist, Mr. Medina understands the needs of the Pharmacy Technician and the important role they play in interacting with Pharmacists, Medical paraprofessionals and the community in the Pharmacy setting.

Answer Sheet

CE Lesson - Compounding

1. It is generally agreed that pharmaceutical products should be prepared with a low percentage of error. The Official Compendium allows a:

   a. Plus or minus 2 percent error
   b. Plus or minus 3 percent error
   c. Plus or minus 4 percent error
   d. Plus or minus 5 percent error

2. Of the following "Graduates," which one is the most accurate?

   a. The Conical Graduate
   b. The Cylindrical Graduate
   c. The Erlemeyer Graduate
   d. The Mortar Graduate

3. With the balance locked in a Class A Prescription Balance, place a weighing paper on each pan and place:

   a. The desired weight on the left pan and the material to be weighed on the right pan
   b. The desired weight on the right pan and the material to be weighed on the left pan
   c. None of the above as a Class A Prescription Balance has only one pan

4. Which type of Mortar & Pestle is preferred for mixing liquids and semi-soft dosage forms?

   a. Porcelain
   b. Wedgewood
   c. Marble
   d. Glass

5. Suspending agents are used as a thickening agent that gives some structure to a suspension and allows easy dispersion of particles. Of the following, which one is a suspending agent?

   a. Alcohol
   b. Tragacanth
   c. Mineral Oil
   d. Heavy Water

6. The importance of Geometric Dilution cannot be overstated. Of the following recipe's, which one would involve Geometric Dilution?

   a. The making of a Suspension to ensure dispersion of particles
   b. The making of an ointment to ensure a homogenous mixture
   c. The making of an elixir to ensure the incorporation of alcohol
   d. The making of a syrup to ensure the incorporation of sugar

7. What is the sensitivity measurement for a Class A Prescription Balance?

   a. 6 milligrams
   b. 30 milligrams
   c. 60 milligrams
   d. 100 milligrams

8. Weights used for the Class A Prescription Balance and other balances usually contain cylindrical weights ranging from:

   a. 1 to 50 mg
   b. 1 to 50 gms
   c. 1 to 50 Kg
   d. 10 to 500 mg

9. In the following formula you are compounding, how much Talc is needed to fill 120 gms?

Nupercainal Ointment	4%
Zinc Oxide	20%
Talc	2%

   a. 1.2 grams
   b. 1.5 grams
   c. 2.0 grams
   d. 2.4 grams

10. Which one of the following statements is false?

a. The Class A Prescription Balance must meet the requirements of the National Bureau of Standards (NBS)
b. Spatulas can be found available in stainless steel, plastic and hard rubber. Which type of spatula to use is dependent on what is being transferred or mixed
c. Most graduates are marked “TD” which means, “to deliver.” 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.
d. Levigating agents are used to reduce particle size and ensure a homogenous mixtue. An example of a levigating agent would be methylcellulose.