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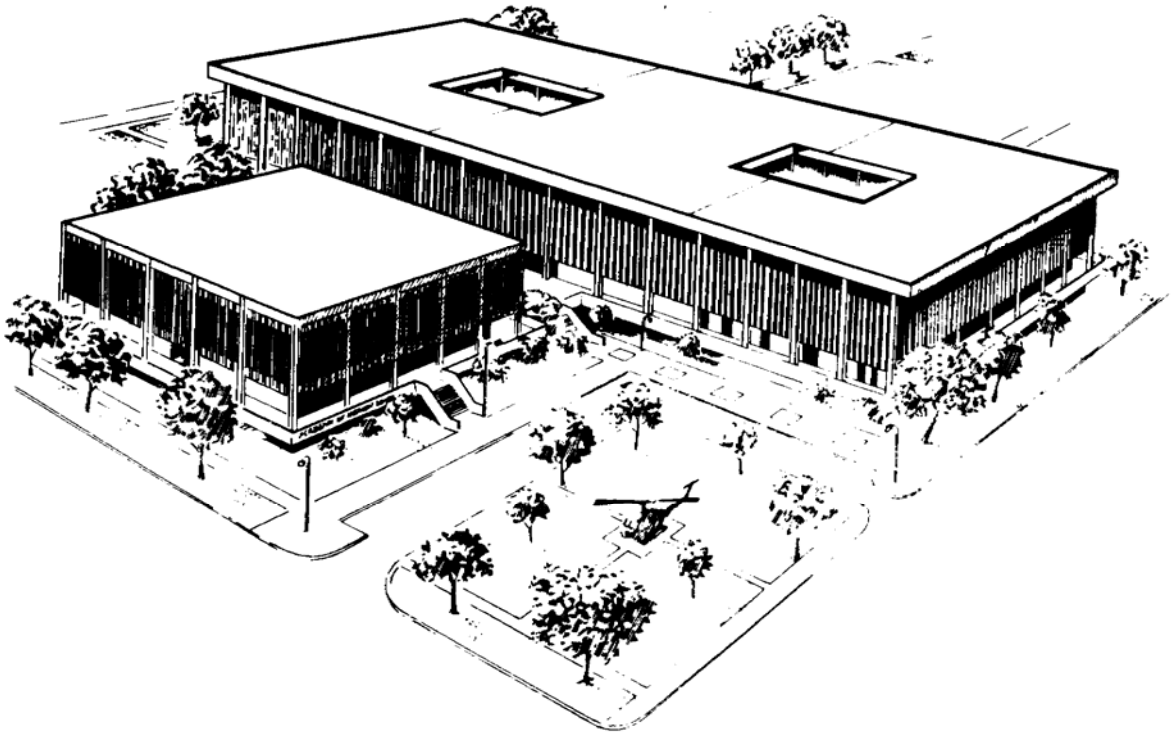

INTRODUCTION TO COMPOUNDING AND MANUFACTURING

SUBCOURSE MD0809 EDITION 200

DEVELOPMENT

This subcourse is approved for resident and correspondence course instruction. It reflects the current thought of the Academy of Health Sciences and conforms to printed Department of the Army doctrine as closely as currently possible. Development and progress render such doctrine continuously subject to change.

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CLARIFICATION OF TRAINING LITERATURE TERMINOLOGY

When used in this publication, words such as "he," "him," "his," and "men" are intended to include both the masculine and feminine genders, unless specifically stated otherwise or when obvious in context.

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CORRESPONDENCE COURSE OF
THE U.S. ARMY MEDICAL DEPARTMENT CENTER AND SCHOOL

SUBCOURSE MD0809

INTRODUCTION TO COMPOUNDING AND MANUFACTURING

INTRODUCTION

In previous subcourses, topics such as prescription interpretation, pharmaceutical calculations, and general chemistry have been discussed. The material in these subcourses has provided you with an excellent background for understanding the ideas and concepts associated with pharmaceutical compounding and manufacturing.

In this subcourse, you will learn about/review the basics of the art and practice of pharmacy – compounding manufacturing. Despite the fact that less compounding and manufacturing is being performed in today's pharmacy, you should still be familiar with the various the various dosage forms being used and how they are prepared.

In subcourses to follow you will continue to gain additional skills and knowledge in the field of pharmacy Specifically, you will look about filling and dispensing prescriptions, performing tasks associated with pharmacy administration, and preparing sterile products.

Subcourse Components:

The subcourse instructional material consists of seven lessons as follows:

Lesson 1, Pharmaceutical Compounding.
Lesson 2, Introduction to Manufacturing, Quality Control, and Prepackaging.
Lesson 3, Classes of Aqueous Preparations.
Lesson 4, Emulsions and Suspensions.
Lesson 5, Medicated Applications.
Lesson 6, Solid Dosage Forms.
Lesson 7, Ophthalmic Preparations.

Here are some suggestions that may be helpful to you in completing this subcourse:

--Read and study each lesson carefully.

--Complete the subcourse lesson by lesson. After completing each lesson, work the exercises at the end of the lesson

--After completing each set of lesson exercises, compare your answers with those on the solution sheet that follows the exercises. If you have answered an exercise incorrectly, check the reference cited after the answer on the solution sheet to determine why your response was not the correct one.

Credit Awarded:

Upon successful completion of the examination for this subcourse, you will be awarded 8 credit hours.

To receive credit hours, you must be officially enrolled and complete an examination furnished by the Nonresident Instruction Section at Fort Sam Houston, Texas.

You can enroll by going to the web site http://atrrs.army.mil and enrolling under "Self Development" (School Code 555).

LESSON ASSIGNMENT

LESSON 1 Pharmaceutical Compounding.

LESSON ASSIGNMENT Paragraphs 1-1 through 1-16.

LESSON OBJECTIVES After completing this lesson, you should be able to:

1-1. Given a pharmaceutical term and a group of definitions, select the most correct definition of that term.

1-2. Given a situation requiring the use of a pharmaceutical reference and a list of references, select the reference most likely to contain information required in the situation.

1-3. Given drawings of several pieces of equipment used to compound prescriptions and the name of a particular piece of such equipment, select the drawing which illustrates the piece of equipment.

1-4. Given the names of several pieces of equipment and/or devices, select the piece of equipment/device which should be used to handle brass weights.

1-5. Given a situation involving the use of a prescription balance and several alternative actions, select the action most appropriate to follow in that situation.

1-6. Given several sequences of procedures, select the sequence of procedures which should be performed when weighing a substance on a prescription balance.

1-7. Given the names of equipment used to measure liquids and a statement concerning the use/accuracy of a particular liquid measuring device, select the name of the equipment which best matches with the statement.

1-8. Given several definitions and the term “TD,” select the definition which best defines the term.

1-9. Given several statements pertaining to the selection of a graduate to measure a liquid, select the statement which best describes a consideration of such a selection.

1-10. Given several drawings, select the drawing that best illustrates the accepted placement of a graduate in relation to the eye when measuring liquids as shown in lesson I.

1-11. Given a drawing depicting the flame produced by either a Bunsen or a Fisher burner with letters pointing toward different parts of the flame, select the letter pointing toward the hottest part of the flame.

1-12. Given a situation which requires the use of a particular type of mortar and pestle and a list of types of mortars and pestles, select the mortar and pestle that should be used in that situation.

1-13. Given a situation involving the filtration of a solution and descriptions of several alternative actions, select the action which should be performed in that situation.

SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 1

PHARMACEUTICAL COMPOUNDING

Section I. INTRODUCTION TO COMPOUNDING

1-1. INTRODUCTION TO COMPOUNDING

a. Several years ago many prescriptions were compounded (carefully made in the pharmacy from various substances) by the pharmacist or pharmacy technician. Today, most drugs are manufactured on a large-scale basis by several companies. Consequently, relatively few prescriptions are compounded in the pharmacy today. Nevertheless, it is important for you to become familiar with some basic information related to the compounding of various dosage forms.

b. This subcourse will provide you with a general background in compounding. To provide you with this background, various dosage forms, their uses, advantages and disadvantages, and the precautions that must be observed with each will be discussed.

c. You should understand that this subcourse should not be used as an authoritative source of compounding information. Should you need such a source of information, seek a reference such as Remington's Pharmaceutical Sciences.

1-2. DEFINITIONS

The following definitions are useful in the field of general pharmacy.

a. **Bulk Manufacturing**. Bulk manufacturing involves the preparation of large quantities of drugs. The large amounts of the prepared product will later be packaged in appropriately sized containers for individual patient use.

b. **Capsule**. A capsule is a solid dosage form that contains a medicament enclosed in either a hard or soft gelatin shell.

c. **Caustic**. A caustic agent is a substance that causes destruction of tissues at the site of application.

d. **Compounding**. Compounding is the preparation of an individual patient prescription. Compounding involves the combination of one or more substances in the amounts specified by the physician or other authorized prescriber.

e. **Douche**. A douche is an aqueous solution used in a part of a cavity of the body for its cleansing and disinfectant action.

f. **Drug**. A drug is any substance, or mixture of substances, which affects living protoplasm. Often, the terms drug and medication are used interchangeably.

g. **Elixir**. An elixir is a clear, sweetened, hydroalcoholic solution designed for oral use.

h. **Emulsion**. An emulsion is a two-phase system consisting of one immiscible liquid uniformly dispersed in another liquid.

i. **Enema**. An enema is a rectal injection most often used to evacuate the bowel.

j. **Expectorant**. An expectorant is an agent that removes mucous from the upper respiratory tract.

k. **Gargle**. A gargle is an aqueous solution used to treat a disease of the mouth or throat.

l. **Liniment**. A liniment is an oily, alcoholic, soapy, or emulsified external preparation intended to be applied with rubbing.

m. **Lotion**. A lotion is a liquid suspension or dispersion intended to be applied externally without rubbing.

n. **Mixture**. A mixture is an aqueous liquid preparation containing suspended insoluble materials intended for internal use.

o. **Ointment**. An ointment is a soft, semisolid preparation containing a medicinal agent intended to be applied externally with or without rubbing.

p. **Paste**. A paste is an ointment-like external preparation consisting of a large proportion of powder.

q. **Pharmaceutical Necessity**. A pharmaceutical necessity is a substance of little therapeutic value (if any) but useful in compounding preparations.

r. **Preservative**. A preservative is a substance added to food products or organic solutions to preserve them from chemical or bacterial action.

s. **Solution**. A solution is a homogeneous mixture of two or more substances.

t. **Spirit**. A spirit is an alcoholic or hydroalcoholic solution of a volatile substance.

u. **Suppository**. A suppository is a solid medicated dosage form intended for insertion into the rectum, vagina, or urethra.

v. **Suspension**. A suspension is a two-phase system consisting of a finely divided solid dispersed in a solid, liquid, or gas.

w. **Syrup**. Syrup is a concentrated aqueous solution of a sugar.

x. **Tablet**. A tablet is a solid medicated dosage form with or without suitable additives.

y. **Tincture**. A tincture is an alcoholic or hydroalcoholic solution prepared from vegetable or chemical materials, usually a10 percent weight/volume (w/v) solution.

1-3. REFERENCES USED IN COMPOUNDING/MANUFACTURING

As previously stated, this subcourse should not be used as an authoritative source of compounding information. It is designed to provide you with a basic background in pharmaceutical compounding. The following sources of information can be used to obtain information useful in compounding and manufacturing:

a. **Remington's Pharmaceutical Sciences**. This text is published by the Mack Publishing Company. The reference deals with the theory and practice of the art of pharmacy. Remington's contains useful information on the many dosage forms of medications present in the pharmacy. Moreover, Remington's contains specific information on the compounding of commonly used pharmaceutical products.

b. **The United States Pharmacopeia (USP) and The National Formulary (NF).** These references contain specific standards and tests for the strength, purity, quality, packaging, and labeling of drugs in the United States. These references are now published together under one cover. The texts are revised every five years. Supplements to the main texts are supplied.

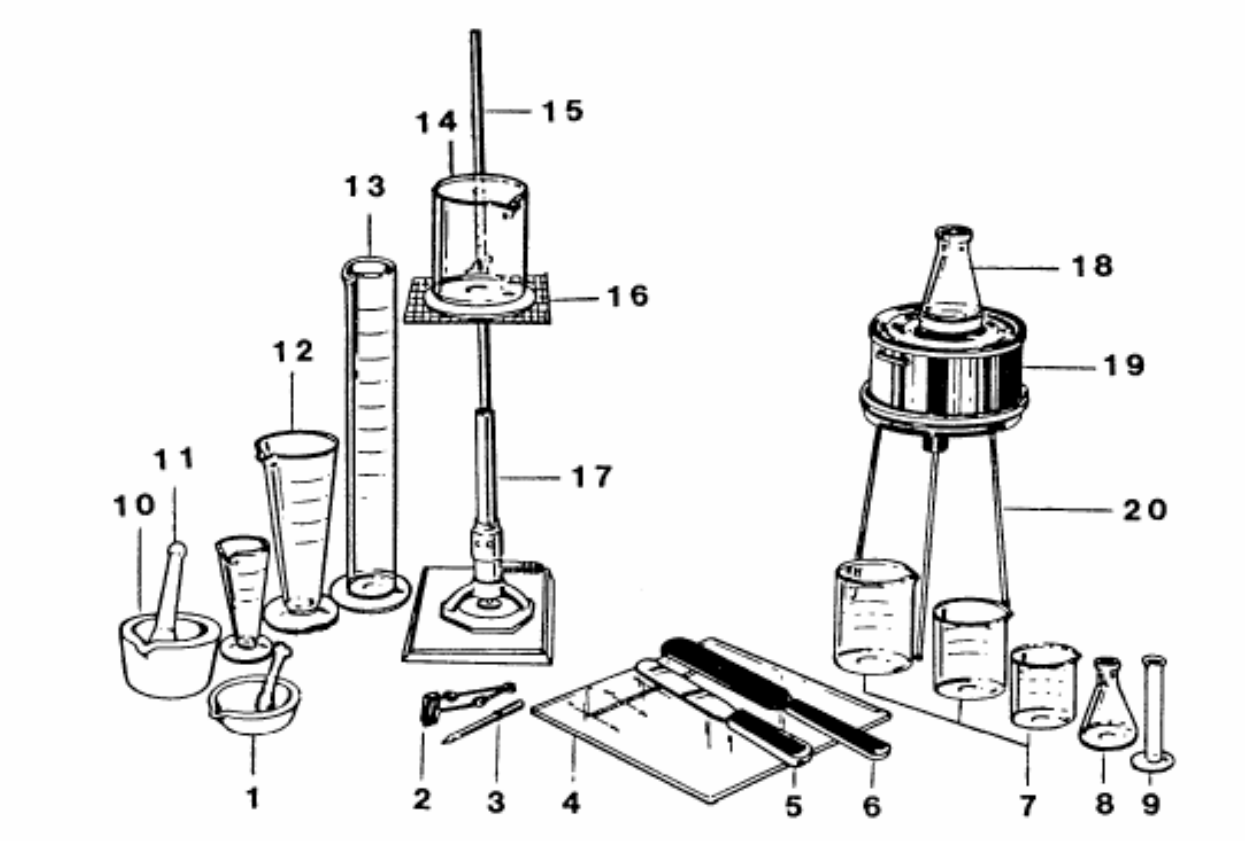
c. **Pharmaceutical Calculations**. This text was written by Mitchell J. Stoklosa. If you frequently review calculations, you will maintain your ability to perform various types of calculations required in pharmaceutical compounding.

1-4. BASIC EQUIPMENT USED IN COMPOUNDING PRESCRIPTIONS

a. Certain equipment is used whenever a prescription is compounded. You must wisely select the equipment that is available to you. See figure 1-1, which shows some equipment found in most hospital pharmacies.

b. Take care to use the equipment wisely. Unwise use of the equipment may produce a product that can be useless or even harmful to the patient. Moreover, unwise use of equipment can lead to equipment damage.

c. Seek assistance whenever you are unsure of the procedures that should be used to compound a product. Pharmacists and experienced pharmacy technicians can frequently provide guidance on tried and tested compounding methods.



1--Glass mortar and pestle
2--Test tube for forceps
3--Medicine dropper
4--Pill tile/ointment slab
5--Metal spatula
6--Rubber spatula
7--Beakers
8--Flask
9--Graduated cylinder
10--Porcelain mortar
11--Pestle
12--Conical graduate
13--Cylindrical graduate
14--Beaker
15--Ring stand with base
16--Bunsen burner
17--Flask
18--Water bath
19--Water bath
20--Tripod

Figure 1-1. Commonly used compounding equipment.

Section II. MEASUREMENT

1-5. SOLID MEASURE

Precise measurement in the compounding of pharmaceuticals is an absolute necessity if the medication is to be beneficial rather than harmful to the patient. Physicists make the following distinction between mass and weight: Mass is the quantity of matter; weight is the force exerted upon a quantity of matter by gravity. Since the force of gravity is not constant at all altitudes and locations, mass is the better term for specifying a quantity of matter. Nonetheless, we often use the word "weight" in the pharmacy to refer to mass. The mass of matter is determined by comparing it to a standard body, using a balance that cancels the effect of gravity.

a. **The Balance**. The balance (see figure 1-2) is the apparatus used for determining mass. It is NOT a scale. A scale measures weight by the use of springs and is influenced by gravity. Weights determined by scales vary from location to location. For example, with a spring scale, a body weighing 1,000 grams (g) in Panama will weigh 1,004 g in Alaska. With a balance, however, a body with a mass of 1,000 g in Panama will have the same reading in Alaska. In its simplest form, the balance consists of a horizontal beam supported in the center. From each end of this beam, a pan is suspended to accommodate the substance to be weighed and the counterbalance. A pointer and a graduated scale are attached to determine when the pans are in balance. Prescription balances are designed to provide the degree of accuracy required for prescription compounding and the manufacture of medicinals. The desired capacity should permit weighing up to 120 g. In actual practice, we do not try to accurately weigh quantities less than 100 mg on a prescription balance, nor do we load the delicate mechanism with weights approaching 120 g. The two most commonly accepted brands of prescription balances are the Torsion Prescription Balance and the Troemner Prescription Balance. Both are acceptable by pharmacy law as being of suitable accuracy and are classified as Class A balances, used for weights less than 120 g. (Larger weights are weighed on less sensitive but accurate balances called Class B balances. Class B balances are optional in the pharmacy.)

b. **Testing a Class A Balance**. The rest point is the reading of a balance after fluctuation of the pointer has stopped. To test a balance, find the rest point when the pans are empty. Then, using proper weighing techniques, set a 10-milligram (mg) weight on only one of the pans. The new rest point should be at least one division removed from the original rest point. The second step is to place one 10-mg weight on the remaining empty pan and find the rest point with a 10-mg weight on each pan. Now we add an additional 10-mg weight to one of the pans, so that we now have 20-mg on one pan and 10-mg on the other. The new rest point should be at least one division removed from the rest point obtained with one 10-mg weight on each pan.

Figure 1-2. Prescription balance.

c. **Weights**. The most accurate balance is worthless unless you use accurate mass standards or weights (see figure 1-3). If either the balance or the weights are inaccurate, an erroneous weighing will result. Good weights are usually made of brass and are available in various styles and shapes. Those that resemble coins in shape should not be used. Weights must be stored in their container at all times when not in use and must not be handled with the fingers. Touching weights with the skin leaves deposits of moisture, body oils, and other foreign particles on the weights and adds to their weight. These deposits may also react with the metal to cause further inaccuracies. Forceps are included in the weight containers for correct handling. USE THEM!

d. **Technique of Weighing**. Before attempting to make a weighing, make certain the balance is level, on a solid support away from drafts, and the pans are in equilibrium (in balance). To level the pans, release the beam lock and allow the pans to swing freely. If the pointer swings an even number of divisions to each side of the scale, your balance is in equilibrium. If, however, the pointer swings unevenly, you must adjust the balance. To bring the balance into equilibrium, raise or lower the adjustable legs at the base of the balance until the proper swing is obtained.

Figure 1-3. Metric weights

(1) Place a powder paper or some other suitable container on each pan and readjust your equilibrium. Powder papers of the same size and consistency may vary in weight as much as 60 mg and can cause errors of up to 30 percent if you do not correct them at the beginning of the weighing.

(2) With the beam locked in stationary position, open the lid and place the desired weight on the right-hand pan (on top of the powder paper). The weights are always placed to the right because on the beam of the balance is a rider (additional fine weight), which may be moved to the right a number of divisions instead of adding extremely tiny weights to the pan. Using this rider, for example, to weigh 264.5-mg, you could either place a 200-mg weight on the right pan and run the rider out to 64.5-mg or simply run the rider out to 264.5-mg. The left pan is convenient for receiving the powders from the container. Use the forceps to place the weights as close to the center of the right pan as possible. Weights placed at the edges of the pan give erroneous readings.

(3) Place on the left pan your best estimate of the required amount of the substance to be weighed. At first, it will be difficult to estimate, but as you become more proficient, you will be able to estimate rather accurately.

(4) Release the beam to see if you have too much, too little or just the right amount of substance on the pan. If the right pan descends and the left rises, you have not enough of the substance being weighed. If, conversely, the left pan descends and the right rises, you have too much of the substance. Lock the securing device and correct the error by adding or removing some of the substance until the balance is in equilibrium.

(5) When the weights on both pans are equal, the balance is in equilibrium, or in balance. This may be determined in more than one way. In the fixed balance method, which is accurate, the pointer remains fixed at the central position when the beam is released. In the swinging balance method, which is more accurate, equilibrium is indicated when the pointer, on release, swings an equal number of divisions to each side of the central position. If allowed to swing until all motion ceases, the pointer will come to rest at the central position. To weigh accurately, however, it is not necessary for the pointer to stop swinging. If, for two or three consecutive arcs, it goes an equal number of divisions to either side, your accuracy is sufficient.

e. **Hints on Weighing**. Following are a few guidelines and checkpoints for the technique of weighing and care of equipment:

(1) Locate your balance in a light place, free from vibration, dust, corrosive vapors, and moisture.

(2) Keep the balance cover closed except when you are using the balance. This prevents damage to the mechanism, extends the effective life of your equipment, and maintains its accuracy. It also keeps out drafts during the weighing process and allows you a more nearly perfect procedure.

(3) Keep your balance clean at all times. Remove any spilled drug or chemical immediately with a soft brush or clean dry towel.

(4) Never weigh materials directly on the pans. Always protect the pans with powder papers or weighing boats. Corrosive substances should be weighed in properly tared, stoppered bottles.

(5) Support the beam with the securing device at all times, except when checking equilibrium, or making a weight determination. This will protect the delicate mechanism from needless wear that leads to inaccuracy. Assure that the pans are supported when adding weights or substances to the pan.

(6) Always keep your weights covered in their proper containers, except during actual use.

(7) Handle weights with forceps only.

(8) Check the weights three times; once, when you remove them from their box and place them onto the pan; again, while they are in use; and finally, when you return them to their box. Form this habit early in your career to avoid serious errors in weighing which can have a disastrous effect on the health and lives of your patients, as well as on your career.

(9) Finally, be as meticulous and accurate in preparing the medication, as you would have another pharmacy specialist be in preparing medication for you.

1-6. LIQUID MEASURE

To measure liquids, you generally measure their volume. Volume is space and so you measure the space they occupy. Customarily, we refer to solids by their weight and to liquids by their volume, but there are a few exceptions to this rule. Glycerin, acids, and many other liquids are received by weight, but are dispensed by volume.

a. **Equipment Used to Measure Volume**. Liquids are measured most frequently in graduates. Occasionally, for greater accuracy, pipettes, burettes, and volumetric flasks may be used. Graduates are of two types: (1) the graduated cylinder, and (2) the conical or pharmaceutical graduate. Both types are available in many sizes and are calibrated in units of volume. Those that are calibrated by hand are more accurate than the machine-marked variety.

(1) Graduated cylinder. The graduated cylinder, calibrated only in milliliters, is widely accepted as the most accurate graduate. It is not practical for general use because it is difficult to clean, dry, fill, and empty.

(2) Conical graduate (pharmaceutical graduate). The conical graduate is the vessel most widely used to determine the volume of a liquid. Although it is slightly less accurate than the graduated cylinder, it is easier to work with and has the advantage of being calibrated in both the metric (milliliters) and apothecary (minims, drams, and ounces) systems.

(3) Receiving versus delivery capacity. Since it is seldom possible to pour all the liquid from the graduate after it has been measured, a differentiation must be made between the receiving capacity (holding capacity) and the delivery capacity of the graduate. Most graduates manufactured today are compensated to read delivery capacity and many are marked “TD” meaning “to deliver.”

(4) Medicine dropper. Too many factors enter into the delivery of a drop of liquid from a dropper to accurately give it any unit of volume.

b. **Technique of Measuring Liquids**. The proper technique for measuring liquids is just as important as the proper technique for weighing solids. It is wise to learn the technique and never deviate from it for any reason.

(1) Choosing the graduate. Choose either a conical or a cylindrical graduate. For most pharmaceutical operations, the conical graduate is better, except where extreme accuracy is required. Choose the proper size graduate for the volume you intend to measure. Obviously, you would select neither a 1-ounce graduate to measure 8-ounces of liquid nor an 8-ounce graduate to measure 1-ounce. A large graduate used to measure a small quantity of liquid will give you a large error. Choose a graduate only a little larger than the amount of liquid you intend to measure. For example, use a 4-ounce graduate to measure 3-1/2-ounces.

(2) Holding the graduate. To measure the liquid, hold the graduate between your thumb and forefinger, allowing the base to rest on your bent middle finger. If you are right-handed, you will probably find it most convenient to hold the graduate in your left hand and left-handers will find the right hand more comfortable.

(3) Holding the bottle. Grasp the bottle to be poured from in the other hand and remove the stopper, cap, or cork with the little finger of the hand in which you are holding the graduate. Make sure the labeled side of the bottle is facing up so that its contents will not drip or spill on the label and deface it.

(4) Holding graduate at eye level. Raise the graduate so that the mark at the desired volume is at eye level. This minimizes the reading error known as error of parallax. Optical illusion distorts the actual level and causes considerable error. Pour the liquid slowly into the graduate until the bottom of the meniscus exactly reaches the required mark (see figure 1-4). The meniscus is the natural curvature of the surface of water.

NOTE: A type of plastic graduate that produces no meniscus is available at some installations. The graduate must still be held at eye level for readings.

(5) Emptying the graduate. After accurately measuring the liquid, pour it into the appropriate container or mixing vessel. Allow sufficient time for it to drain. This is especially important with viscous liquids such as syrup and glycerin. Clean the graduate as soon as possible after use. Graduates washed immediately after use or put to soak with a detergent are easier to clean than those on which the substance has dried and hardened are. The most important reason for immediate cleaning is to have the graduate available for immediate reuse.

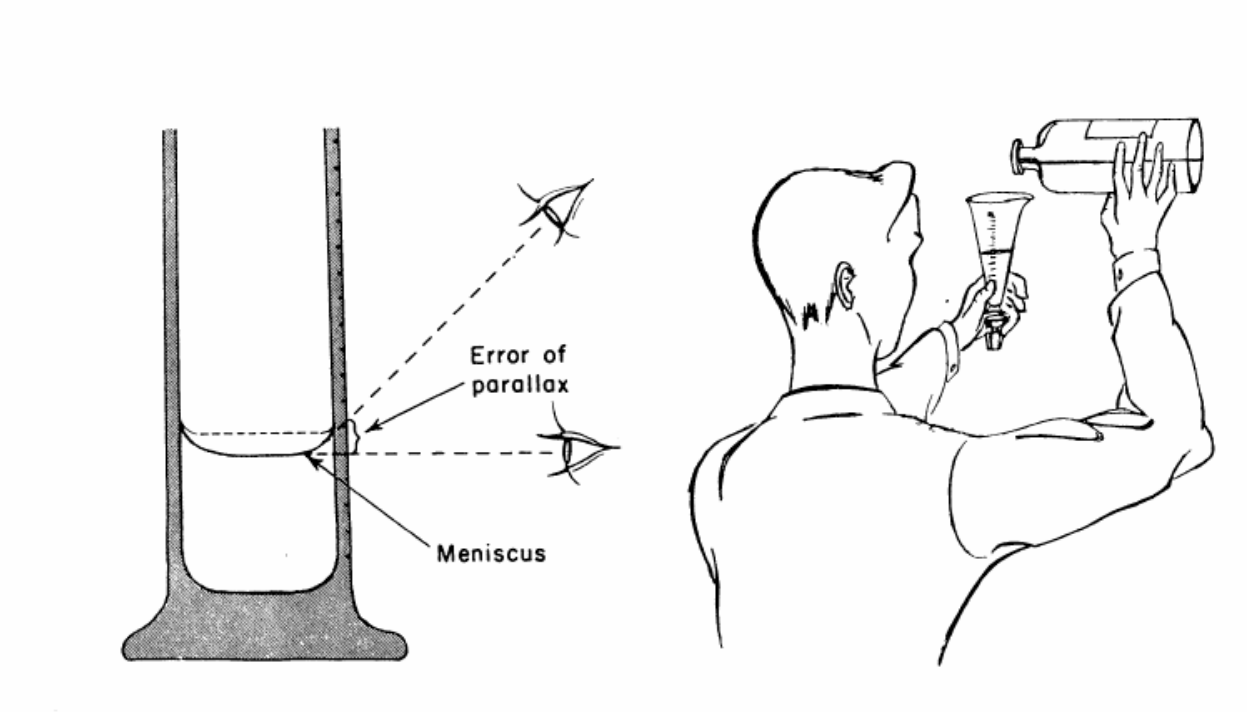


Figure 1-4. Reading the graduate.

Section III. HEAT

1-7. METHODS

There are many applications for the use of heat in the pharmacy. Many pieces of equipment are available to produce, distribute, and regulate this heat.

a. **Types of Gas Burners**. Gas is the most frequently used source of heat in small-scale manufacturing. The Fisher and Bunsen burners are two types of gas-utilizing apparatus available to your pharmacy section (see figure 1-5). The Fisher burner produces higher temperatures and is easier to operate under normal circumstances. In bulk compounding, the Fisher burner will save you a considerable amount of time because it will heat large volumes of material much faster than the Bunsen burner.

(1) Adjusting the flame. At the base of the burner are vents through which the air enters. This air is mixed with incoming gas. The amount of air is adjusted by screwing the tube up or down on a threaded base. The amount of gas is regulated by turning the disk (gas valve) at the base. Together, these devices can be used to control the size and intensity of the flame.

(2) Temperatures available. It is important for you to know the temperature at various points within the flame. This knowledge will enable you to heat substances at the proper temperature and to position the substance to be heated to attain the hottest temperature. Figure 1-6 compares the flame temperatures of both burners at different levels within each flame.

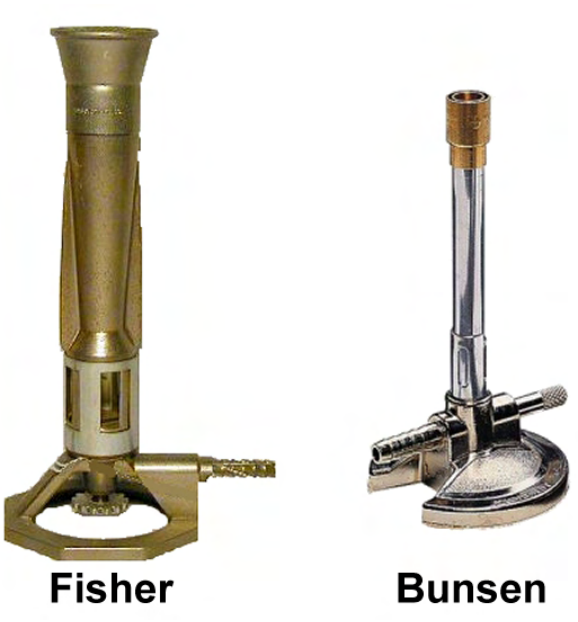


Figure 1-5. Fisher and Bunsen burners.

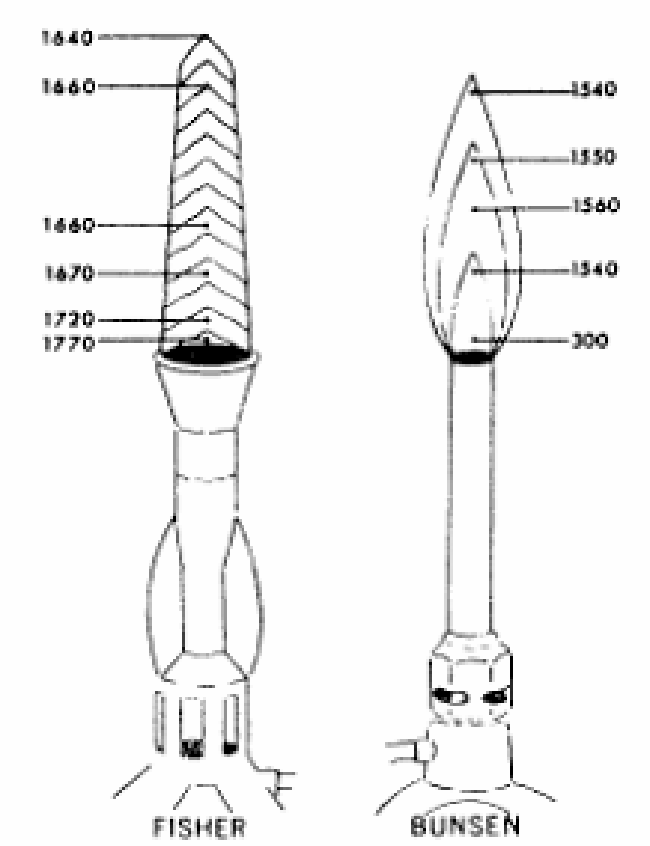


Figure 1-6. Temperature comparison of the Fisher and Bunsen burners (numbers denote temperatures in degrees Fahrenheit).

b. **Apparatus Utilizing Electricity**. Electrical heating is clean and easy to use but its temperature cannot be closely controlled. Never place your glass containers directly on an electrical heating device because they may break.

1-8. REGULATION OF HEAT

a. Many medicinal products are affected by the application of excessive heat. Further, it is advantageous to be able to control the level of heat you are applying to a particular substance or product. Baths of various types are used to control and distribute heat.

b. Water baths are probably the most frequently used means to regulate and control heat. Water baths consist of copper or Monel metal containers equipped with a lid from a number of concentric rings of the same material. The concentric rings can be removed or added to permit adjustments for various sizes of flasks or beakers. A short horizontal tube is provided near the top of the bath for the escape of steam. Since both the water in the bath and the steam arising from it are under atmospheric pressure, the highest temperature obtainable is 100º C. If the heating is to be continued for a long period, the water lost by evaporation must be replaced.

1-9. PHYSICAL PROCESSES INVOLVING HEAT

a. **Evaporation**. In pharmacy, evaporation signifies the process of applying heat to drive off a portion of the liquid as a vapor. Such a liquid may consist of a solution of a nonvolatile substance in water, alcohol, or other solvent. The purpose of evaporation is to concentrate the solution or to obtain the solute in dry form. Evaporation may be hastened by:

(1) Using a shallow evaporating dish which exposes as large a surface of the solution as possible.

(2) Stirring the solution constantly which allows the free escape of vapors and ensures the even heating of the entire quantity of liquid.

(3) Using sufficient heat.

(4) Reducing atmospheric pressure.

b. **Distillation**. Distillation is the separation of the constituents of a liquid mixture by vaporization and subsequent condensation of the vapors. Such a separation is made possible by the different boiling points of the various volatile constituents**.**

c. **Sublimation**. This is the process of distilling volatile solids. The product obtained from the process is called a sublimate. Sublimation is similar to distillation, but there is no intermediate liquid state. The volatile solid evaporates and is resolidified.

d. **Desiccation**. Desiccation is a dehydration process for removing moisture from solid substances. The moisture thus driven off is called hygroscopic moisture as distinguished from moisture that is chemically combined, as in water of crystallization. The process should be conducted at the lowest effective temperature; this may be accomplished by exposing the substance to a dry atmosphere at ordinary temperature or by placing it in a drying oven at a moderate temperature.

Section IV. COMMINUTION

1-10. INTRODUCTION

Comminution is a mechanical process in which the particle size of a solid is reduced or the degree of subdivision of a solid is increased. Substances may be comminuted for the following three reasons:

a. To increase the rate of solution of solids.

b. To increase the ease and thoroughness of extraction of animal and vegetable drugs.

c. To obtain a uniform powder or mixture of powders that can be used to prepare medicinal solids in their most desirable form.

1-11. METHODS OF COMMINUTION

Comminution is a broad term that includes several methods or processes of accomplishing reduction in particle size. Pulverization is the reduction of a substance to a powder. Several methods used to comminute solids follow:

a. **Trituration**. Trituration is the process of reducing the particle size of a substance by rubbing it in a mortar with a pestle. Trituration is also a correct term for the intimate mixing of two or more powders together, the rubbing of light, fluffy powders into heavier, denser, and more compact composition. In either sense of its use, trituration is more than a grinding or mixing. It is a technique widely used in pharmacy. Trituration is a crushing-mixing process, accomplished with circular motion of the pestle under pressure.

(1) Technique. To properly triturate a substance and ensure best pulverization and intimate mixing, you should use the following technique:

(a) Place the substance to be comminuted, thoroughly mixed, or defluffed in the mortar.

(b) Start at the center of the mortar, with downward pressure on the pestle and a circular motion of very small diameter; rub the substance between the pestle and the mortar. Gradually increase the diameter of the circles until you reach the side of the mortar and then decrease the diameter of the circles gradually until the center is again reached.

(c) Scrape the powder frequently with a spatula from the sides of the mortar and from the bottom of the pestle.

(d) Continue the trituration until the desired comminution is attained or until the powders are thoroughly mixed.

(2) Types of mortars.

(a) Wedgewood mortars. Wedgewood mortars are most commonly used for trituration because their rough surface aids in the rubbing. They are difficult to keep clean, however, because of their porous surface. Dyes must never be triturated in a wedgewood mortar as the color will become permanently affixed to the vessel and threaten future powders.

(b) Glass mortars. Glass mortars are preferred for comminuting substances that stain and for dissolving granular or crystalline substances that require rubbing to aid in their solution.

(c) Porcelain mortars. Porcelain mortars are useful in making emulsions or solutions not involving staining substances. Porcelain mortars and pestles are fragile, as are glass and wedgewood, and any heavy crushing should be performed using other methods.

(3) Spatulas. Although spatulas play a more important role in other procedures and techniques (for example, levigation), they are used in scraping down the sides of the mortar in trituration. A spatula resembles a knife in having a handle and a blade. The blade, which varies in size, is very flexible and dull. The spatula is probably the most frequently used tool in the pharmacy. Spatulas may be made of metal (preferably stainless steel) or of hard rubber. The type used depends upon the substances being processed.

b. **Pulverization by Intervention**. This is the process of reducing a substance to a powder by dissolving it in a small amount of volatile solvent and triturating until dry. For example, to powder camphor, dissolve the camphor in a small amount of alcohol, triturate until the alcohol evaporates and the resulting substance will be a powder.

c. **Levigation**. Levigation is a process by which the particle size of substances is reduced by making a paste of the substances, using a liquid in which they will not dissolve such as water, glycerin, or mineral oil. This paste forms the basis for a medicinal. This process may be accomplished either in a shallow mortar or on an ointment slab. Levigation is a valuable process in compounding ointments that include a powder. It makes a much more elegant, non-gritty product in a considerably shorter time than does simple incorporation.

Section V. SEPARATION

1-12. INTRODUCTION

There are frequent occasions in pharmacy when it is necessary to separate the individual components of substances. Such procedures may be performed after preparation (for example, filtering out foreign particles) or may be performed while making the preparation as in the formation of a desired precipitate.

1-13. SEPARATION BY HEAT

a. We will now discuss the separation of different substances, not just the separation of different particle sizes. The first of these is separation by heat. Previously, in the section dealing with the application of heat, we defined a number of processes; of those processes, the following are methods of separation:

(1) Evaporation.

(2) Distillation.

(3) Sublimation.

(4) Desiccation.

b. These processes have already been discussed and will not be reviewed here. Besides, the use of heat to separate substances, precipitation, filtration, and collation may also be used.

1-14. PRECIPITATION

Precipitation is the process of separating, by physical or chemical change, solid particles from a previously clear liquid. The separated solid is called the precipitate; the causative agent, the precipitant; and the liquid that remains in the vessel above the precipitate, the supernatant liquid. A precipitate may, because it is less dense, float to the top instead of settling to the bottom. Crystallization is a type of precipitation in that the precipitate takes on a crystalline structure. That is to say, the solid formed has definite structure. Granulation, or the production of fine crystals, is a disturbed or interrupted crystallization. Large crystals are prevented from forming by constant agitation during the cooling. Instead of a single mass being formed, a fine granular mass results.

1-15. FILTRATION

a. Filtration is a process for separating suspended or sedimental solid material. A porous barrier made of paper, sand, charcoal, or other insoluble material allows the liquid to pass, but prevents the solid from moving with the liquid. Medications must be filtered before dispensing under the following circumstances:

(1) Undissolved material is present in the solution.

(2) The solution to be dispensed is cloudy.

NOTE: Sometimes the active ingredients in a solution will hasten or “fall-out” of solution. Thus, filtering the solution will remove the undissolved material or cloudiness; however, that material is the drug the physician wanted the patient to receive. When you see undissolved material in a solution that has been supplied to you, you should seek the assistance of someone (that is, a pharmacy officer) to determine the wisdom of using a particular solution.

b. The usual filtering apparatus in the pharmacy consists of filter paper and a glass funnel. The funnel may be either smooth or ribbed glass. The ribbed funnel hastens the filtration process by providing a passageway for the liquid.

c. There are numerous ways of folding filter paper. The most commonly used folds are the “plain filter,” made from the circular filter paper sheet by two simple folds, and the “pharmaceutical” or “plaited” filter. To prepare a “plaited” filter, start by folding the circular paper into quarter sections. At the beginning of a quarter section, make folds of approximately one-half inch in alternating directions until the quarter section is completely folded. Fold the remaining quarter sections in the same manner. The creases must NOT be too sharp; otherwise, the fibers will be loosened. Furthermore, the creases must NOT go all the way to the center because this will seriously weaken the filter.

d. Prior to filtering and solution, the filter paper (no matter what the fold) should be wetted with sterile water. See figure 1-7, which illustrates the two methods of folding filter paper.

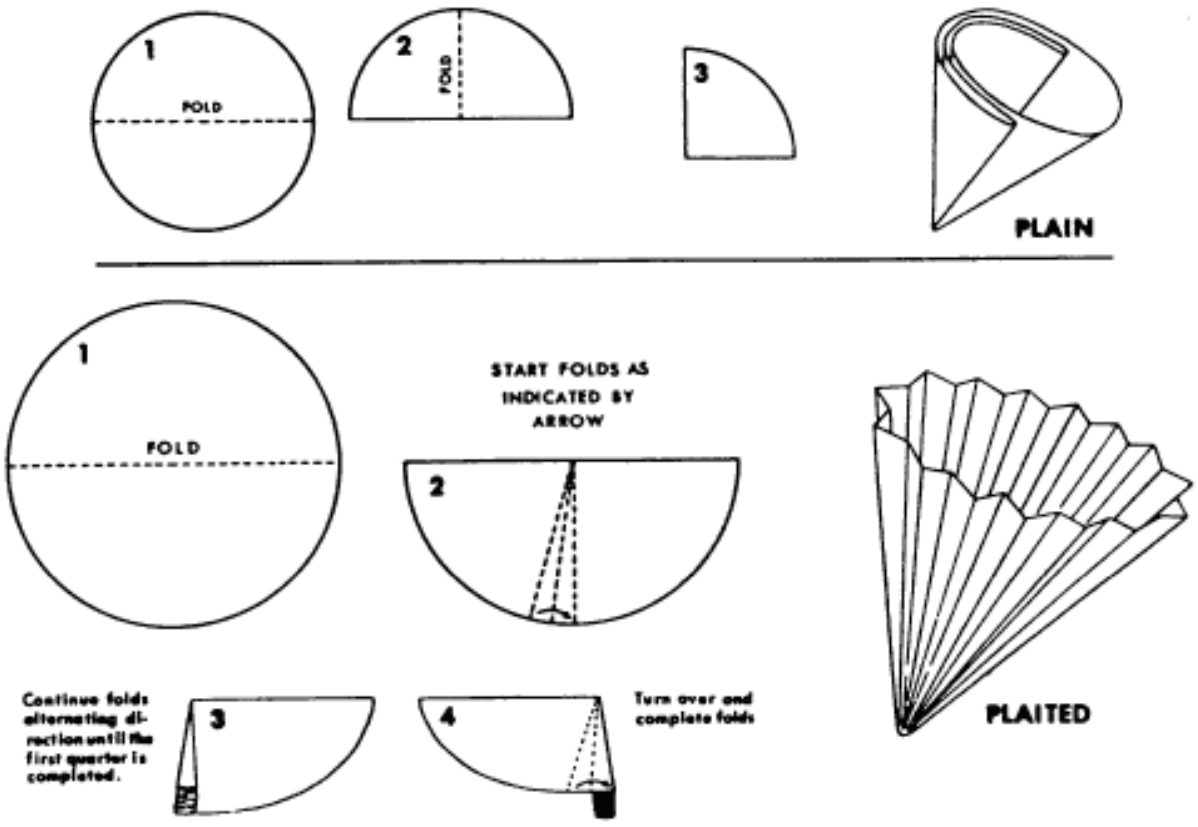


Figure 1-7. Two methods of folding filter paper.

1-16. COLATION

Colation, or straining, is essentially the same process as filtration. The difference between colation and filtration is the particle size to be separated and consequently the nature of the intervening media. The process of collation separates a coarser solid from a liquid by passing the mixture through a cloth, gauze, or long-fibered cotton. Collation is more realistic than filtration for removing foreign particles from syrups and other slow-flowing liquids.

Continue with Exercises

EXERCISES, LESSON 1

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or best completes the incomplete statement or by writing the answer in the space provided.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. You wish to locate specific information on the tests for purity of a particular chemical substance. Select the title of the reference most likely to provide you with this information.

   a. Pharmaceutical Calculations by Stoklosa.

   b. Remington's Pharmaceutical Sciences.

   c. The United States Pharmacopeia and The National Formulary.

   d. The Physicians' Desk Reference.

2. You wish to locate specific information on the compounding of an ointment. Select the title of the reference most likely to provide you with this information.

   a. Remington's Pharmaceutical Sciences.

   b. The Physicians Desk Reference.

   c. Pharmaceutical Calculations by Stoklosa.

   d. The United States Pharmacopeia and The National Formulary.

3. Select the device you should use when adding or removing brass weights from a balance:

   a. #6 scapel.

   b. Pestle.

   c. Fingers.

   d. Forceps.

4. Select the step you should perform before weighing a substance on a prescription balance.

    a. Ensure the balance is rated “Class B”.

    b. Ensure the balance is level.

    c. Ensure that your brass weights have been polished.

    d. Ensure that the beam is unlocked.

5. Select what act you should do when adding or removing any substance to/from the prescription balance:

    a. Ensure the substance is noncaustic.

    b. Cover the balance with a plastic sheet for protection of the pans.

    c. Remove the powder papers from the pans.

    d. Lock the securing device to prevent damage to the beam.

6. Select the type of equipment that is widely accepted as being the most accurate device to measure liquids.

    a. The conical graduate.

    b. The graduated cylinder.

    c. The Thompson-Miller beaker.

    d. A flask.

7. Select the type of liquid measuring device that is the most widely used in pharmacy.

    a. The graduated cylinder.

    b. The beaker.

    c. The flask.

    d. The conical graduate.

8. Select the meaning of “TD” in reference to glassware.

    a. To deliver--the volume read is the volume delivered.

    b. To deliquesce-the graduate is used to measure fluids that increase in volume due to their absorption of water.

    c. To dispose--the graduate is used to measure highly viscous fluids that are difficult to pour.

    d. To dispense--the graduate is designed to pour directly into a prescription bottle.

9. Select the statement that best describes a consideration involved in the selection of a graduate to measure a liquid.

    a. Choose a graduate that is slightly larger than the volume of liquid you intend to measure.

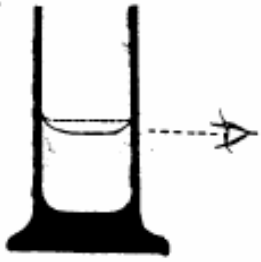
    b. Choose only a graduated cylinder that is calibrated in both metric and apothecary units.

    c. Select a graduate with a wide mouth since it is easier to pour liquids into.

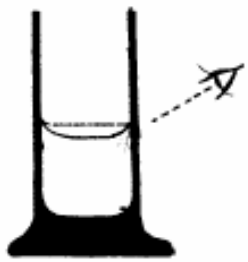
    d. Choose a graduate made from smoked glass in order to protect the liquid from light.

10. From the four illustrations below, select the illustration that best demonstrates the proper placement of the graduate in relation to the eye when measuring liquids.

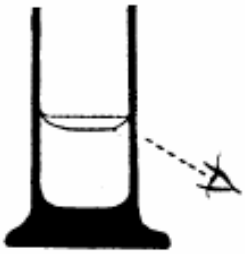
a.



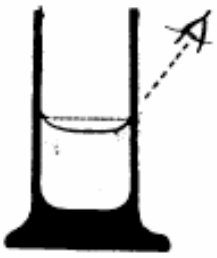
b.



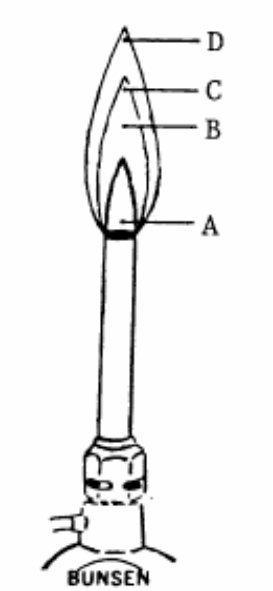
c.



d.



11. From the illustration below, select the letter that is pointed to the hottest part of the flame produced by the Bunsen burner.



a. A.

b. B.

c. C.

d. D.

12. Select the most correct definition of the term desiccation.

a. The separation of the constituents of a liquid mixture.

b. A dehydration process for removing moisture from solids.

c. The process of distilling volatile solids.

d. The process of removing solids from a liquid in the presence of heat.

13. Select the most correct definition of the term comminution.

    a. The process of combining two different substances.

    b. The mechanical process used to purify drugs.

    c. The physical process used to decrease the volume of a solid.

    d. A mechanical process in which the particle size of a solid is reduced.

14. Select the type of mortar that should be used to reduce the size of iodine crystals. Remember that iodine crystals are likely to stain most materials.

    a. Wedgewood.

    b. Porcelain.

    c. Glass.

    d. 50-mm.

15. You are about to dispense a solution to a patient when you observe a precipitate in the bottom of the prescription bottle. Select, from the actions below, the best action to take in this situation:

    a. Attach a “Shake Well” auxiliary label and dispense the prescription.

    b. Pour the solution into an amber-colored bottle.

    c. Add more liquid to the bottle so the substance will go into solution.

    d. Seek the assistance of a pharmacy officer to determine whether the prescription should be dispensed.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 1

1. c (para 1-3b)
2. a (para 1-3a)
3. d (para 1-5d(2))
4. b Ensure the balance is level. para 1-5d)
5. d (para 1-5d(4))
6. b (para 1-6a(1))
7. d (para 1-6a(2))
8. a (para 1-6a(3))
9. a (para 1-6b(1))
10. a (para 1-6b(4))
11. b (para 1-6)
12. b (para 1-9d)
13. d (para 1-10)
14. c (para 1-11a(2)(b))
15. d (para 1-15(2) Note)

End of Lesson 1

LESSON ASSIGNMENT

LESSON 2	Introduction to Manufacturing, Quality Control, and Prepackaging.
LESSON ASSIGNMENT	Paragraphs 2-1 through 2-9.
LESSON OBJECTIVES	After completing this lesson, you should be able to:

2-1. Given a group of definitions, select the definition of the term pharmaceutical (bulk) manufacturing.

2-2. Given a group of statements, select the most appropriate justification of pharmaceutical (bulk) manufacturing.

2-3. Given a group of possible uses, select the use of the Bulk Compounding Formula Record (Master Formula Card) as presented in Lesson 2.

2-4. Given a group of possible actions, select the action that must be performed to order controlled substances for manufacturing purposes using the DOD Prescription Form (DD 1289).

2-5. Given the type of product to be prepared and/or the use of a particular piece of manufacturing equipment and a list of names of pieces of manufacturing equipment, select the piece of equipment to be used to prepare the product and/or described.

2-6. Given a group of definitions, select the definition of quality control as presented in Lesson 2.

2-7. Given a group of tests, select the test used to perform quality control procedures.

2-8. Given a group of statements, select the definition of pharmaceutical prepackaging as presented in Lesson 2.

2-9. Given a group of statements, select the most appropriate justification of pharmaceutical prepackaging as presented in Lesson 2.

2-10. Given a list of labeling information, select the piece of essential information that should appear on labels for prepackaging dispensing units.

2-11. Given a list of labeling information, select the piece of essential information that should appear on labels for prepackaged drugs in nondispensing units.

SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 2

INTRODUCTION TO MANUFACTURING, QUALITY CONTROL, AND PREPACKAGING

Section I. PHARMACEUTICAL MANUFACTURING

2-1. BACKGROUND INFORMATION

a. **Definition**. Pharmaceutical (bulk) manufacturing is the compounding of large quantities of a pharmaceutical product that is designed to be dispensed to more than one patient.

b. **Justification**. There are two primary justifications for pharmaceutical (bulk) manufacturing in the modern pharmacy.

(1) In some cases, a commercially available product can be manufactured in the pharmacy in order to save money. Obviously, all the costs (for example, ingredients, equipment, and manpower) must be considered when this justification is used.

(2) In other circumstances, a product is manufactured because an equivalent product is not commercially available. For example, if a dermatologist were to frequently prescribe a particular ointment that is not commercially available, it would be cost effective to manufacture this product rather than to compound each individual prescription for the ointment.

2-2. FORMS USED IN THE MANUFACTURING SECTION

As you might anticipate, there are no specific manufacturing forms that are used in all U.S. Army medical treatment facilities (MTFs). This subcourse will merely provide guidance on the types of information that should be contained on certain forms used within the manufacturing section. Again, it is important to realize that forms are tailored to meet the individual needs of a particular MTF. So, the forms you see in your MTF might contain more or less information than you see on the forms used to train students in the 91Q Pharmacy Specialist Course.

a. **Bulk Compounding Formula Record (Master Formula Card)**. The Bulk Compounding Form (Master Formula Card) is the official recipe for a particular product compounded in the pharmacy. The Master Formula Card (see figure 2-1) contains specific information on the preparation, packaging, and labeling of a product. Observe that the Master Formula Card is designed to tell you <u>everything</u> you need to know about the preparation of a product.

BULK COMPOUNDING FORMULA RECORD

Product		Lot Number
GUAIFENESIN EXPECTORANT	15,000 ml	

ORIGINAL FORMULATION	Prepared By / Date	Reviewed By / Date	Approved By / Date
	MAJ S. Sollars 5 Feb 84	MAJ R. Pozyk 6 Feb 84	COL R. Sikora 7 Feb 84

SECTION A

ITEM	Ingredients		Manufacturer	Lot No.	EXP Date	Amount used	Weighed By / Checked By
1	Guaifenesin	300 Gm					
2	Simple Syrup, USP	9,600 ml					
3	Chloroform	45 ml					
4	Menthol	1.5ml					
5	Wild Cherry Flavor	10.5ml					
6	Amaranth, 1% Solution	30 ml					
7	Ethyl Alcohol, USP	750 ml					
2	Purified Water, qsad	15,000 ml					

PROCEDURE:

1. Dissolve the guaifenesin in 2,000 ml of hot purified water while the water is still on the hot plate.
2. In a separate container, dissolve the chloroform, menthol, and wild cherry flavor in the ethyl alcohol.
3. Add and mix both solutions together in the Alsop Mixer/Filter Unit and agitate thoroughly. Then add the simple syrup.
4. Add the amaranth solution to the solution.
5. Add sufficient purified water to make the product measure 15,000 ml.
6. Filter the product using #51 filter pads.
7. Package and label the product.

Theoretical Yield	Actual Yield	Reason for Loss	
15,000 ml			
Packaging	**Cost/Batch**	**Cost/Unit Container**	**Time Required**
125-4 oz amber bottles	----------	----------	4 hours

Compounded By	Packaged By	Labeled By

Label Directions:

ALAMO ARMY HOSPITAL
FT. DAVY CROCKETT, TEXAS 221-2351

FOR

GUAIFENESIN EXPECTORANT

Take 1 to 2 teaspoonsful every 3-4 hours for cough.

Control # 503384

KEEP OUT OF REACH OF CHILDREN

FOR INSTRUCTIONAL USE ONLY

QUALITY CONTROL PROCEDURES:

a. Specific Gravity of final product is 1.044

b. pH of final product is 6.3

Approved for release by Quality Control

Signature: Date:

Figure 2-1. Bulk Compounding Formula Record (Master Formula Card).

b. **Batch Sheet**. The Batch Sheet (see figure 2-2) is a work copy of the Bulk Compounding Formula Record (Master Formula Card). The Batch Sheet is to be used to record entries (that is, initials of the individual who weighed the ingredients) during the manufacturing process. Thus, the Batch Sheet provides a means to ensure the product is prepared according to the established standards.

BATCH BULK COMPOUNDING FORMULA RECORD SHEET

Product: GUAIFENESIN EXPECTORANT — 15,000 ml — Lot Number: 503384

ORIGINAL FORMULATION | Prepared By: SFC S. Sollars Date: 5 Feb 84 | Reviewed By: MAJ R. Pettyjr 6 Feb 84 | Approved By: COL R. Sikora Date: 7 Feb 84

SECTION A

ITEM	Ingredients		Manufacturer	Lot No.	EXP Date	Amount used	Weighed By / Checked By
1	Guaifenesin	300 Gm	International Chemical	37GP6	May 86	300Gm	CH / SS
2	Simple Syrup, USP	9,600 ml	AAH	GP642	Jul 85	9,600ml	CH / SS
3	Chloroform	45 ml	Thompson Chemical	90001A	Jan 87	45ml	CH / SS
4	Menthol	1.5ml	Mallinckrodt Chem.	A5033JK	Aug 85	1.5ml	CH / SS
5	Wild Cherry Flavor	10.5ml	Dewey Products Co.	J21214	Sept 85	10.5ml	CH / SS
6	Amaranth, 1% Solution	30 ml	Gentry Corp.	K373654	June 85	30ml	CH / SS
7	Ethyl Alcohol, USP	750 ml	Haelen, Inc.	1PAA21	Feb 86	750ml	CH / SS
8	Purified Water, qsad	15,000 ml	AAH	390114	Mar 85	qsad 15,000ml	CH / SS

PROCEDURE:

1. Dissolve the guaifenesin in 2,000 ml of hot purified water while the water is still on the hot plate.
2. In a separate container, dissolve the chloroform, menthol, and wild cherry flavor in the ethyl alcohol.
3. Add and mix both solutions together in the Alsop Mixer/Filter Unit and agitate thoroughly. Then add the simple syrup.
4. Add the amaranth solution to the solution.
5. Add sufficient purified water to make the product measure 15,000 ml.
6. Filter the product using #51 filter pads.
7. Package and label the product.

Theoretical Yield	Actual Yield	Reason for Loss	
15,000 ml	123 - 4 fl oz bottles	N/A Equipment	
Packaging	**Cost/Batch**	**Cost/Unit Container**	**Time Required**
125-4 oz amber bottles	----------	----------	4 hours

Compounded By: SFC Steve Sollars | Packaged By: SP5 Carl Hallmark | Labeled By: SFC Steve Sollars

Label Directions:

ALAMO ARMY HOSPITAL
FT. DAVY CROCKETT, TEXAS 221-2351

FOR

GUAIFENESIN EXPECTORANT
Take 1 to 2 teaspoonsful every 3-4 hours for cough.

Control # 503384

KEEP OUT OF REACH OF CHILDREN
FOR INSTRUCTIONAL USE ONLY

QUALITY CONTROL PROCEDURES:

a. Specific Gravity of final product is 1.044

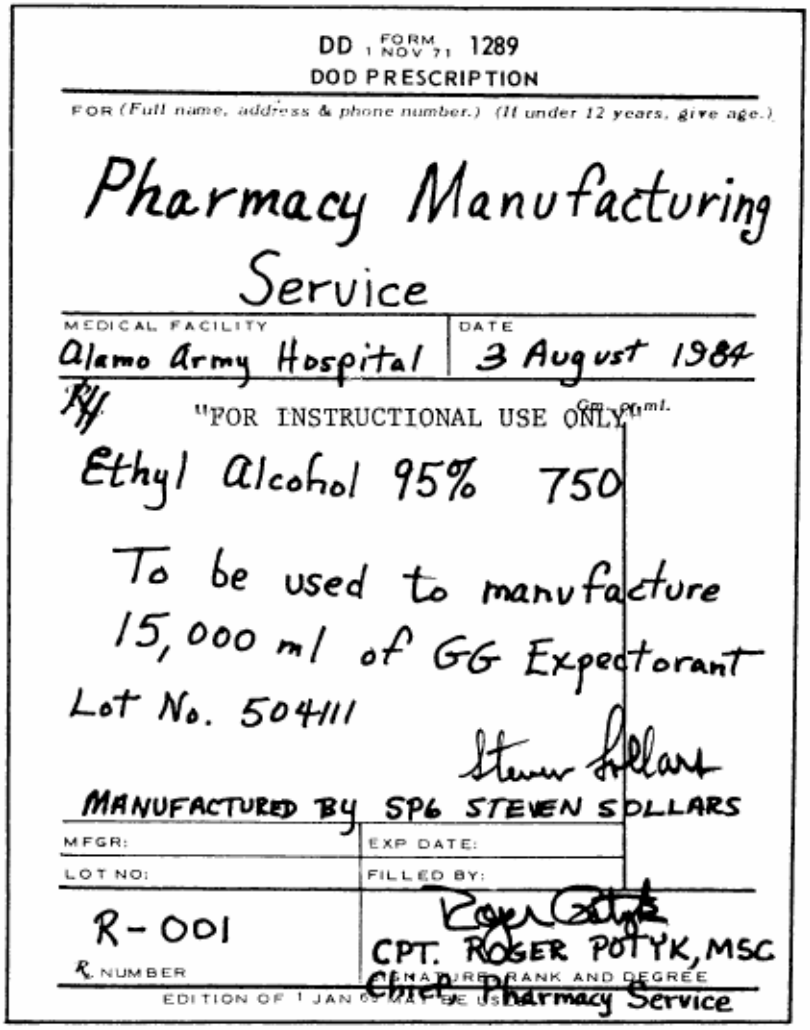
b. pH of final product is 6.3

Approved for release by Quality Control

Signature: Date:

Figure 2-2. Batch Sheet.

c. **Prescription Form (DD 1289)**. Department of Defense (DD) Form 1289 (see figure 2-3) is the official prescription form used in the U.S. Army. In the manufacturing section, the DD Form 1289 is used to order controlled substances used to manufacture products. To order controlled substances for manufacturing purposes, the R_x must be lined out. The R_x is lined out because the prescription order is not intended for an individual patient. The DD Form 1289 is not signed by a physician in this particular case. Instead, the DD Form 1289 is prepared by manufacturing personnel, signed by a pharmacy officer, and carried to the controlled drug area where it is filled.



DD FORM 1 NOV 71 1289

DOD PRESCRIPTION

FOR (Full name, address & phone number.) (If under 12 years, give age.)

Pharmacy Manufacturing Service

MEDICAL FACILITY: Alamo Army Hospital

DATE: 3 August 1984

Rx "FOR INSTRUCTIONAL USE ONLY"

Ethyl Alcohol 95% 750 ml.

To be used to manufacture 15,000 ml of GG Expectorant

Lot No. 504111

Steven Sollars

MANUFACTURED BY SP6 STEVEN SOLLARS

MFGR:

EXP DATE:

LOT NO:

FILLED BY:

R-001

R NUMBER

Roger Potyk

CPT. ROGER POTYK, MSC

SIGNATURE, RANK AND DEGREE

Chief Pharmacy Service

EDITION OF 1 JAN 65 MAY BE USED

Figure 2-3. DD Form 1289 used to acquire controlled substance (ethyl alcohol) for manufacturing purposes.

2-3. EQUIPMENT USED IN THE MANUFACTURING SECTION

A manufacturing section usually contains certain types of equipment. There are numerous brands and variations of these items available. The specific pieces of equipment presented and discussed in this area of the subcourse are representative samples of what you could see in a pharmacy manufacturing area.

a. **Alsop Mixer/Filter Tank.** The Alsop mixer/filter tank (figure 2-4) is probably the most frequently used piece of manufacturing equipment. As the name implies, it is both a mixer tank and a filter tank. The mixer tank can be used to prepare a variety of pharmaceutical products (for example, solutions). The filter tank can be used to filter solutions.

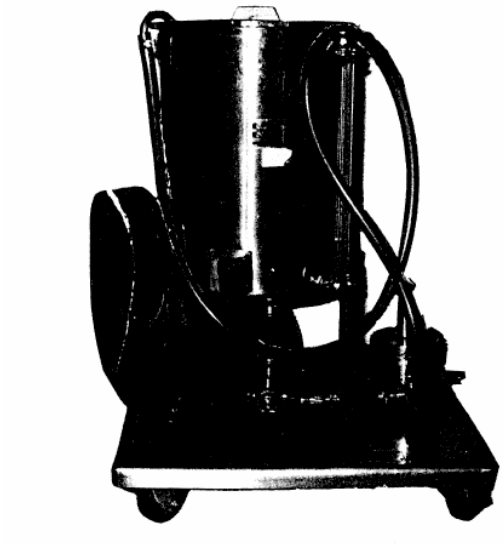


Figure 2-4. Alsop mixer/filter tank.

b. **Eppenbach Colloid Mill.** The Eppenbach colloid mill (figure 2-5) is used to reduce the particle size of ingredients and to make preparations such as suspensions, lotions, magmas, and emulsions. The colloid mill should never be operated without tap water flowing through the cooling hoses because the grinding knives could be damaged due to heat caused by friction.

c. **Erweka Power Unit.** The Erweka power unit (with sliding rheostat) (figure 2-6) is the driving force for three commonly used attachments.

(1) The three roller mill (ointment mill) (figure 2-7). The three-roller mill is used in the preparation of ointments, salves, pastes, and other similar products.

(2 The agitator (figure 2-8). The agitator consists of a stirring kettle and an agitating driving unit. It is used for stirring, agitating, and beating all kinds of liquids, emulsions, suspensions, and similar mixtures.

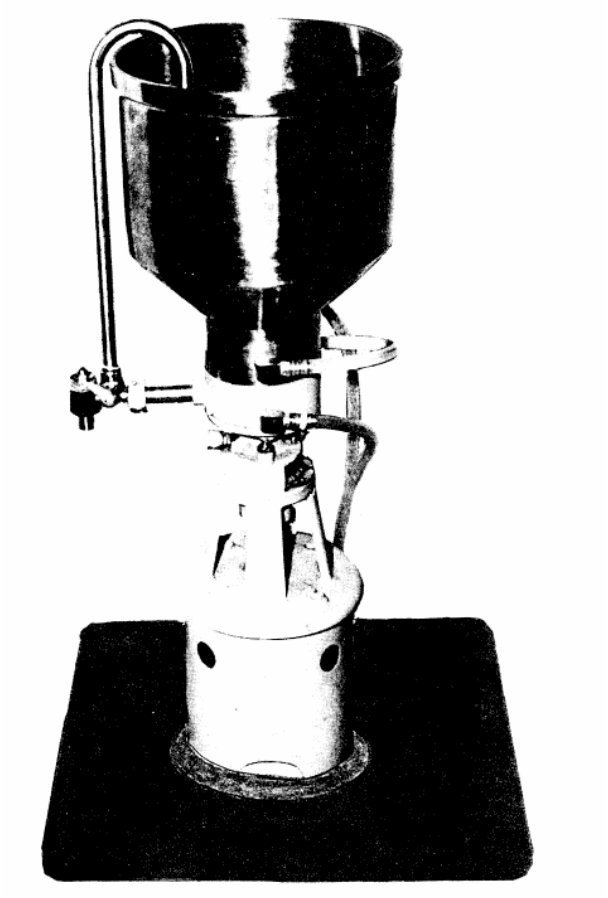


Figure 2-5. Eppenbach colloid mill.

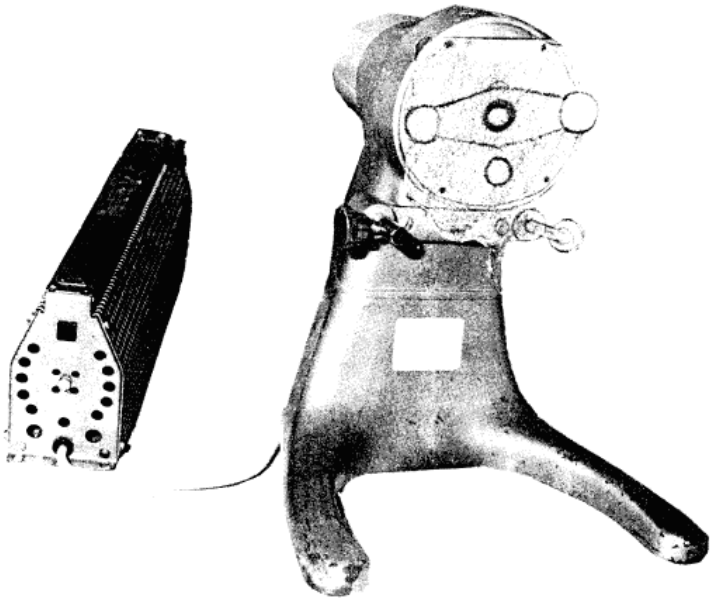


Figure 2-6. Erweka power unit.

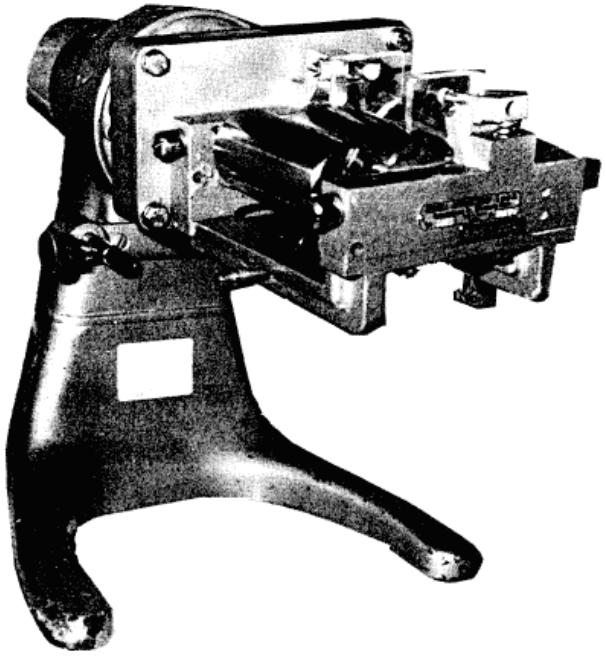


Figure 2-7. The three-roller mill (ointment mill).

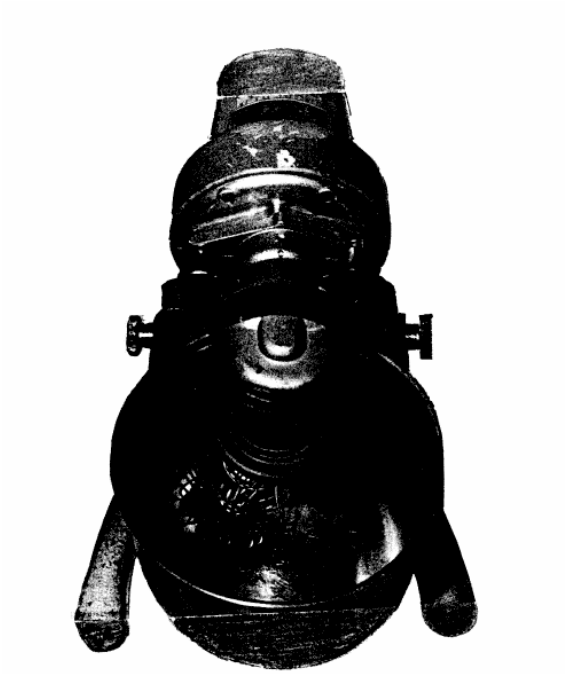


Figure 2-8. The agitator.

(3) The kneader-mixer (figure 2-9). The kneader-mixer serves two functions. It is equipped with a stirrer for use with liquids to be mixed and a kneading wood roller attachment with which heavy viscosity materials can be kneaded. The unit is also supplied with a scraper that removes material from the kettle walls and returns it to the center of the container to ensure proper mixing. The stainless steel kettle rotates and the mixing attachments move along the inside of the kettle at the same time. A stirring beater attachment is used to intermix-lighter viscosity materials.

Figure 2-9. The kneader-mixer.

d. **The Vacuum 3 SF (Suction Flask) Bottle Filler**. The vacuum 3 SF (suction flask) bottle filler (figure 2-10) is used primarily for the repackaging of bulk liquid preparations into smaller, more suitably sized containers for individual patient use. Examples of products repackaged in this manner are milk of magnesia, mouthwash, kaolin with pectin, and cough syrup.

Figure 2-10. The vacuum 3 SF (suction flask) bottle filler.

e. **The Sobar Labeling Machine.** The Sobar labeling machine (figure 2-11) is a printing press. This label printing machine has its own type which can be used to set any letter/number order required to print labels for a manufactured or a repackaged product. A sample label depicting how the product must be labeled will appear on the Master Formula Card for that product. This sample label is used as an example for the printing of the required number of labels.

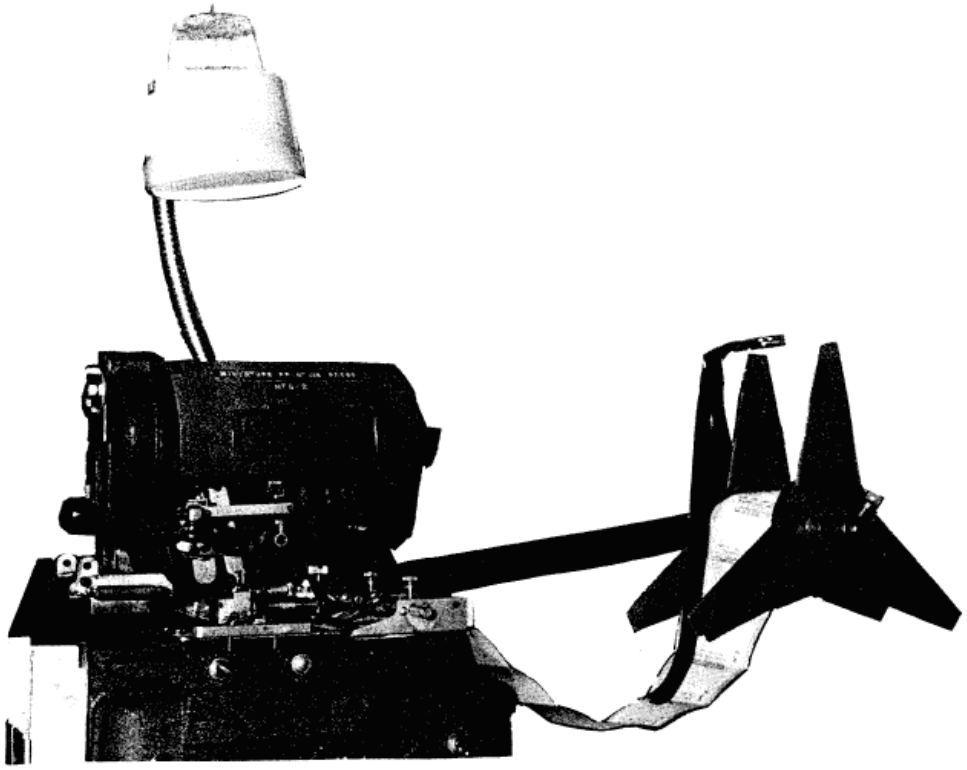


Figure 2-11. The Sobar labeling machine.

Section II. QUALITY CONTROL

2-4. INTRODUCTION TO QUALITY CONTROL

Quality control is an important term in pharmacy. Patient lives, as well as the reputation of the pharmacy, depend upon quality control procedures. This section will focus on quality control procedures that can be used in the manufacturing section.

a. **Definition**. Quality control is a process which builds high quality into a product by ensuring the use of good raw materials and the adherence to a rigid set of good manufacturing practices during every step of the manufacturing process. Quality control begins with checking raw ingredients and continues by performing many checks throughout the production process. Quality control ensures that the correct number of labels are printed and used for each batch of a manufactured product. Quality control procedures are used to ensure that the manufactured product meets the standards that have been established for its use.

b. **Quality Control Information**. Each particular manufactured product has certain characteristics that can easily be determined. Originally, when the product was first formulated, these characteristics (for example, specific gravity, refractive index, and/or pH were determined and established on the Master Formula Card for that particular product (see figure 2-12). Always be familiar with this area of the Master Formula Card because it clearly describes the standards the product must meet before it can be dispensed to patients.

2-5. QUALITY CONTROL TESTS

The following quality control tests are used to evaluate manufactured products to ensure their quality and purity for patient use.

a. **Visual Inspection**. With visual inspection, the ingredients and the final products are carefully examined for purity and for appearance.

b. **Specific Gravity**. Specific gravity is defined as the weight (in grams) of a substance per unit volume (in milliliters). Each prepared product has a characteristic specific gravity. A device called a hydrometer tube is used to measure the specific gravity of a liquid preparation. If the specific gravity of a prepared product does not meet established standards for that product, the product must not be dispensed to patients.

c. **Refractive Index**. The refractive index is a measure of the degree of the bending of light, which passes through the substance. The refractive index of a substance is measured with a device called a refractometer. Again, each product has an established refractive index.

d. **pH**. The pH of a substance refers to its acidity or alkalinity. As with the other quality control measures, each particular product has its own characteristic pH. The pH of a product can be determined by using pH papers or pH meters.

BULK COMPOUNDING FORMULA RECORD

Product: GUAIFENESIN EXPECTORANT — 15,000 ml — Lot Number: 503384

ORIGINAL FORMULATION | Prepared By: SFC S. Sollars Date: 5 Feb 84 | Reviewed By: MAJ R. Pettigill Date: 6 Feb 84 | Approved By: COL R. Sikora Date: 7 Feb 84

SECTION A

ITEM	Ingredients		Manufacturer	Lot No.	EXP Date	Amount used	Weighed By / Checked By
1	Guaifenesin	300 Gm	International Chemical	37GP6	May 86	300Gm	CH / SS
2	Simple Syrup, USP	9,600 ml	AAH	GP 6A2	July 85	9,600ml	CH / SS
3	Chloroform	45 ml	Thompson Chemical	90801A	Jan 87	45ml	CH / SS
4	Menthol	1.5ml	Mallinckrodt Chem.	A5033JK	Aug 85	1.5ml	CH / SS
5	Wild Cherry Flavor	10.5ml	Davey Products Co.	J21214	Sept 85	10.5ml	CH / SS
6	Amaranth, 1% Solution	30 ml	Gentry Corp.	K373654	June 85	30ml	CH / SS
7	Ethyl Alcohol, USP	750 ml	Hazlon, Inc.	1PAA21	Feb 86	750ml	CH / SS
8	Purified Water, qsad	15,000 ml	AAH	390114	Mar 85	qsad 15,000ml	CH / SS

PROCEDURE:

1. Dissolve the guaifenesin in 2,000 ml of hot purified water while the water is still on the hot plate.
2. In a separate container, dissolve the chloroform, menthol, and wild cherry flavor in the ethyl alcohol.
3. Add and mix both solutions together in the Alsop Mixer/Filter Unit and agitate thoroughly. Then add the simple syrup.
4. Add the amaranth solution to the solution.
5. Add sufficient purified water to make the product measure 15,000 ml.
6. Filter the product using #51 filter pads.
7. Package and label the product.

Theoretical Yield	Actual Yield	Reason for Loss	
15,000 ml	123 - 4 fl oz bottles	N/A Equipment	
Packaging	**Cost/Batch**	**Cost/Unit Container**	**Time Required**
125-4 oz amber bottles	----------	----------	4 hours

Compounded By: SFC Steve Sollars | Packaged By: SP5 Carl Hellmich | Labeled By: SFC Steve Sollars

Label Directions:

ALAMO ARMY HOSPITAL
FT. DAVY CROCKETT, TEXAS 221-2351

FOR

GUAIFENESIN EXPECTORANT

Take 1 to 2 teaspoonsful every 3-4 hours for cough.

Control # 503384

KEEP OUT OF REACH OF CHILDREN

FOR INSTRUCTIONAL USE ONLY

QUALITY CONTROL PROCEDURES:

a. Specific Gravity of final product is 1.044

b. pH of final product is 6.3

Approved for release by Quality Control

Signature: Date:

Figure 2-12. Quality control information on Bulk Compounding Formula Record (Master Formula Card).

Section III. PHARMACEUTICAL PREPACKAGING

2-6. INTRODUCTION TO PREPACKAGING

Many pharmacies operate a prepackaging section. This section will focus on the function of this important area.

a. **Definition**. Pharmaceutical prepackaging is defined as the repackaging of bulk supplied drugs into containers which contain quantities of the drug which are more suitable for individual patient use.

b. **Justification**. The following are two reasons of justification:

(1) Cost. Many preparations can be purchased in bulk quantities at fairly low prices. Then, the medication can be repackaged in smaller containers that contain enough of the medication for one patient. For example, during the “flu and cold” season, the demand for nasal decongestants increases tremendously. Physicians who prescribe this type of medication usually write for the same number of capsules to be dispensed. Further, physicians normally give the same dosage directions to each patient who is to receive that particular drug. Thus, money can be saved if the nasal decongestant is prepackaged and labeled.

(2) Time. Prepackaged drugs can be dispensed quickly and easily with the same professional checks as you would give any prescription. Thus, as in the last example dealing with the “flu and cold” season, time savings are quickly realized when hundreds of patients suddenly appear at the front window to obtain the same drug.

2-7. EQUIPMENT USED IN A PREPACKAGING SECTION

Many pharmacies use the Versacount prepackaging machine (see figure 2-13). This machine can be calibrated to place a specific number of capsules or tablets in a drug container.

2-8. LABELING REQUIREMENTS FOR PREPACKAGING DISPENSING UNITS

The pharmacy service in most hospitals is not in operation 24 hours a day. Thus, when situations arise (for example, in a clinic or in the emergency room) in which drugs must be dispensed when the pharmacy is closed, the medications must be dispensed and labeled as per Army Regulation (AR) 40-2. To prevent medication errors, properly labeled prepackaged medications are sent to various clinics or to the emergency room. This type of prepackaged medication is designed to be dispensed to the patient by authorized prescribers.

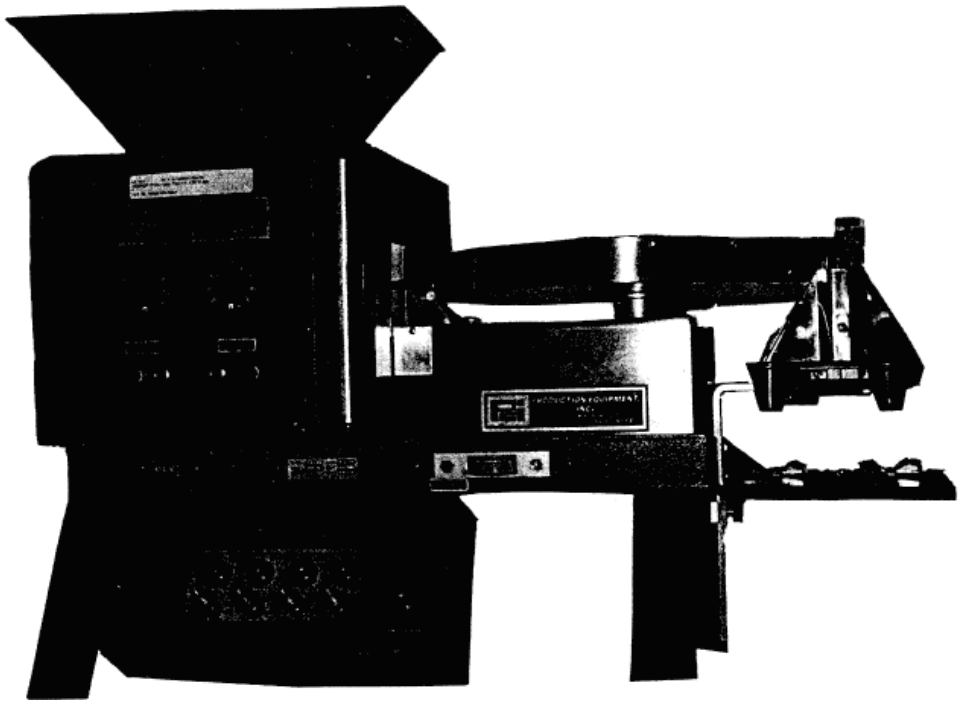


Figure 2-13. Versacount prepackaging machine.

a. **Essential Labeling Information**. All labels should have the essential information below.

(1) Name of patient (blank space is provided).

(2) Date medication is dispensed (blank space is provided).

(3) Directions to the patient (blank space is provided).

(4) Name of drug, its strength, and quantity dispensed.

(5) Lot number of the drug.

(6) Drug manufacturer.

(7) Expiration date of the drug.

(8) Prescriber's name (blank space is provided).

NOTE: Although a blank space is provided for the prescriber's name, this information is optional.

b. **Sample Label Format**. See figure 2-14 for a sample label format. In order to dispense this type of pre-pack, the information is filled in by the authorized prescriber and dispensed to the patient.

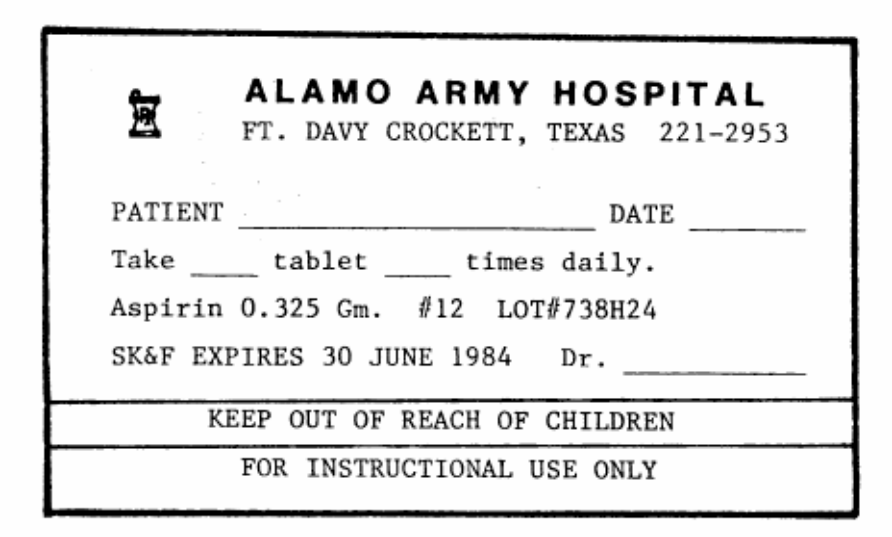


Figure 2-14. Sample label format for prepackaging dispensing units.

2-9. LABELING REQUIREMENTS FOR PREPACKAGED DRUGS IN NONDISPENSING UNITS

This type of prepackaging is used to stock the ward, clinic, or emergency room with authorized medication. This method is very advantageous because it helps these personnel to easily identify medications, assists in identifying expired medications, and facilitates the recall of drugs once they leave the pharmacy. Wards, clinics, and emergency rooms are authorized up to a 2-week stock level of medications from the pharmacy service. This method of repackaging breaks the bulk issue containers into more usable containers that can hold a 2-week supply of medication.

a. **Essential Labeling Information**. Make sure each label has the following information.

(1) Generic name of the medication, trade name of the medication in parentheses (if applicable), the strength of the medication, and the quantity of medication present in the container.

(2) Manufacturer of the medication.

(3) Lot number of the medication.

(4) Expiration date of the medication.

b. **Sample Label Format**. See figure 2-15 for a sample label format. To dispense this type of prepack, the label must be prepared and affixed to the container. It is important for you to understand that the container <u>is not</u> dispensed to patients.

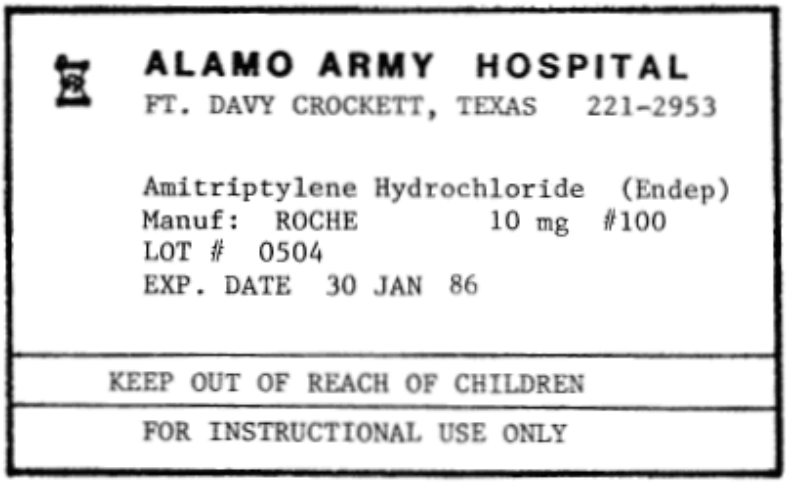


Figure 2-15. Sample label format for prepackaged drugs in nondispensing units.

Continue with Exercises

EXERCISES, LESSON 2

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or best completes the incomplete statement or by writing the answer in the space provided.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Select the most correct definition of the term bulk manufacturing.

   a. The preparation of a small amount of a pharmaceutical product designed to be dispensed to one patient.

   b. The preparation of large quantities of a pharmaceutical product designed to be dispensed to more than one patient.

   c. The preparation of large volumes of external pharmaceutical preparations designed to be dispensed to one patient.

   d. The preparation of small amounts of a pharmaceutical product designed to be dispensed to more than one patient.

2. From the group of justifications below, select the most appropriate justification for pharmaceutical (bulk) manufacturing in the modern pharmacy.

   a. The bulk manufacturing program insures that all people are kept working all the workday.

   b. The bulk-manufacturing program insures that products meet USP/NF standards.

   c. The bulk-manufacturing program insures that the required quality control steps have performed.

   d. The bulk-manufacturing program can help the pharmacy save money.

3. Select the action that must be performed to order controlled substances manufacturing purposes using DD Form 1289.

    a. The DD Form l289 must be lined out.

    b. The R_x must be lined out.

    c. The specific gravity of the liquid substances must be written on the form.

    d. The patient information area must be lined out.

4. From the list of names of pieces of equipment, select the piece of equipment used to prepare products such as suspensions, lotions, magmas, and emulsions.

    a. The kneader-mixer.

    b. The Eppenbach colloid mill.

    c. The Erweka power unit/three roller mill.

    d. The kneader-mixer.

5. From the list of tests below, select the test used as a quality control measure.

    a. Specific gravity test.

    b. Kuder-Richardson Formula 21 test.

    c. Osmotic pressure test.

    d. Chemical precipitation test.

6. From the group of definitions below, select the most correct definition of the term pharmaceutical prepackaging:

    a. Repackaging drugs in unlabeled bottles for ease of storage.

    b. Repackaging drugs in flexible containers for safety purposes.

    c. Repackaging of tablets or capsules supplied in bulk-quantities for purposes of storage safety.

    d. Repackaging of bulk supplied drugs into containers that contain quantities of the drug that are more suitable for individual patient use.

7. From the list of justifications below, select the one that best justifies pharmaceutical prepackaging.

   a. Effective uses of personnel keeps people busy repackaging drugs.

   b. Time-prepackaged drugs can be dispensed professionally and quickly.

   c. Drug safety-drugs can be secured easier.

   d. Legal aspects-pharmacy personnel need not be concerned with laws and regulations when dispensing prepackaged drugs.

8. From the list of advantages below, select the advantage of proper labeling of prepackaged drugs in nondispensing units.

   a. lit assists in identifying expired medications.

   b. It prevents loss of medications.

   c. It reduces the cost of medications.

   d. It insures the drug's-potency will be extended.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 2

1. b (para 2-1a)
2. d (para 2-1b(1))
3. b (para 2-2c)
4. b (para 2-3b)
5. a (para 2-5b)
6. d (para 2-5a)
7. b (para 2-6b(2))
8. a (para 2-8)

End of Lesson 2

LESSON ASSIGNMENT

LESSON 3 Classes of Aqueous Preparations.

LESSON ASSIGNMENT Paragraphs 3-1 through 3-17.

LESSON OBJECTIVES After completing this lesson, you should be able to:

3-1. Given a group of definitions, select the definition of the term solution.

3-2. Given a list of possible components, select the part(s) of a solution.

3-3. Given a group of possible advantages, select the advantage of solutions as a dosage form as presented in Lesson 3.

3-4. Given a group of possible disadvantages, select the disadvantage of solutions as a dosage form.

3-5. Given several possible methods of preparing solutions, select the method of solution preparation.

3-6. Given a list of considerations/situations, select the consideration/situation in which heat should not be used to prepare solutions.

3-7. Given a group of definitions, select the definition of the term saturated solution.

3-8. Given a group of definitions, select the definition of stock solution as presented in Lesson 3.

3-9. Given a list of types of information, select the information which should appear on the label of stock preparations.

3-10. Given a group of definitions, select the definition of the term syrup as presented in Lesson 3.

3-11. Given a list of percentage concentrations, select the percentage of sucrose in syrup, USP.

3-12. From a group of definitions, select the definition of the term spirit as presented in Lesson 3.

3-13. From a group of definitions, select the definition of the term tincture as presented in Lesson 3.

3-14. Given a group of statements, select the statement that best pertains to the storage of tinctures.

3-15. From a group of definitions, select the definition of the term elixir as presented in Lesson 3.

3-16. From a group of definitions, select the definition of the term liniment as presented in Lesson 3.

SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 3

CLASSES OF AQUEOUS PREPARATION

Section I. SOLUTIONS

3-1. INTRODUCTION

a. **Importance of Solutions**. Many drugs are supplied in solution form. Consider intravenous (IV) solutions. Many IV solutions are administered to patients who are in military or civilian hospitals across the United States. Further, think of the number of prescriptions written every fall and winter for decongestant solutions. Although most outpatient pharmacy services dispense more tablets and capsules than solutions, it is easy to see that solutions are still important in the field of pharmacy.

b. **Definition of Solution**. A solution is a homogeneous mixture of two or more substances. Typically, a drug is placed in water.

c. **Parts of a Solution**. A solution consists of two parts:

(1) Solute. The solute is usually the active ingredient. It is the substance that is dissolved in the second part of the solution, the solvent. The solute is usually present in a lower proportion than is the solvent.

(2) Solvent. The solvent serves as the vehicle for the solute. That is, the solute is dissolved in the solvent.

3-2. USES OF SOLUTIONS

Solutions may be used either internally or externally. Intravenous solutions are intended for internal use. Mouthwashes are intended for external use. They are not intended to be swallowed. Solutions have many pharmaceutical uses. Immediately following are some uses of solutions.

a. Collyria-use in the eye.

b. Collutoria--for use as mouthwashes.

c. Collunaria--for use in the nose or nasopharynx.

d. Douches--for instillation into one of the body cavities.

e. Enemas--for instillation into the rectum.

f. Gargles--for use in the mouth and throat.

g. Inhalations or Aerosols--to be vaporized and inhaled into the respiratory tract.

h. Injections--for injection, by hypodermic needle and syringe, beneath the skin.

i. Sprays and Drops--solutions are sprayed or dropped on affected areas.

j. Washes--for application to the skin for their local effect.

3-3. ADVANTAGES OF SOLUTIONS

The advantages of solutions are given below.

a. They are easily administered (especially as oral medication for children).

b. They provide uniform dosage since they are uniform preparations.

c. They are easy to measure if accurate measuring instruments are used.

d. They are usually pleasing in appearance to the patient because of their color and clarity.

e. They have a more rapid onset of action, when administered orally, than tablets or capsules.

NOTE: Tablets and capsules must disintegrate or dissolve before they can become effective.

3-4. DISADVANTAGES OF SOLUTIONS

The disadvantages of solutions are given below.

a. The tastes of medications in solution are more pronounced. Some are almost impossible to overcome.

b. There is a possibility of rapid deterioration and chemical reaction in solutions.

c. Inaccurate measurements may result when using inaccurate measuring instruments such as teaspoons.

NOTE: Not all teaspoons will measure the same volume of fluid.)

d. Solutions are more difficult to store and carry than solid preparations.

3-5. PREPARATION OF SOLUTIONS

a. It is impossible to fully discuss the preparation of solutions in this subcourse. If you desire a thorough discussion of this topic, you should seek an appropriate reference (that is, Remington's Pharmaceutical Sciences).

b. The following are three basic methods of preparing official solutions:

(1) Simple solution. An example is Potassium Iodide Solution, NF.

(2) Chemical reaction. An example is Magnesium Citrate Solution, NF.

(3) Extraction. This method is rarely used in the modern pharmacy.

NOTE: Because of special considerations and procedures which must be used in the preparations of ophthalmic solutions, ophthalmic solutions will not be discussed in this lesson. See Lesson 7.

3-6. SIMPLE SOLUTIONS

When a single substance is dissolved in a solvent, a simple solution results. Simple solutions are used both as complete medicinal agents and as vehicles or ingredients in more complex preparations.

a. **Preparation of the Simple Solution**. For the most part, few difficulties are encountered with simple solutions. Preparing them generally consists of mixing the solute with the solvent and stirring or shaking until the solute goes into solution.

(1) Readily soluble substances. Readily soluble substances are added to a portion of the solvent in a graduate and stirred with a glass-stirring rod until solution is effected. The remainder of the solvent is then added and the combination stirred further until the finished volume is reached. The resulting solution should be filtered, if necessary.

(2) Slowly soluble substances. With slowly soluble or very insoluble solutes, best results are obtained by placing the solute in a mortar and adding portions of the solvent to it with constant trituration. Fine powders, particularly, tend to float on the surface if they are added to the solvent. They should be placed in a mortar, moistened with a very small amount of solvent, and then brought up to volume with trituration.

b. **Forms of Solids**. The solids that you will dissolve are usually available in three commercial forms: powdered, granular, and crystalline. The finer a drug is in subdivision, the more quickly it will be soluble.

c **When Heat is Inadvisable**. Heating aids solution and may be desirable when preparing solutions. But heat is inadvisable when:

(1) The solvent will deteriorate from heat.

(2) A volatile or aromatic liquid must be added to the newly formed solution which, if hot, would result in loss of the volatile substance.

(3) The solute may be totally or partially decomposed by the heat, as is the case with chloral hydrate or sodium bicarbonate.

(4) It is possible for a supersaturated solution to occur by accident. Supersaturated solutions are not suitable for dispensing.

d. **Mixtures of Liquids**.

(1) Potent liquids. When small quantities of potent liquids are prescribed in solution, part of the solvent should be placed in a graduate that is capable of measuring the final volume of the intended preparation. The powerful liquid is then measured carefully in a smaller graduate and added to the solvent in the larger graduate. The graduate used to measure the potent liquid is then rinsed with successive portions of the solvent into the larger graduate until the proper volume is attained. In the same manner, viscid liquids, such as glycerin, should be rinsed from their measuring vessel into the final solution with portions of the solvent. Using this method, you can be reasonably sure that the final preparation contains the desired amount of the active ingredient.

(2) Shrinkage. When two or more liquids are mixed, the resulting volume may be less than the sum of the two portions. The "shrinkage" is more noticeable with some liquids than others. Alcohol and water shrink about five percent when mixed.

e. **Solvents**. The universal solvent, water, is the first solvent we generally think of, but many other solvents are used in pharmaceuticals, such as glycerin, alcohol, alcohol-water mixture, propylene glycol, and oils. Other solvents less commonly used are carbon tetrachloride, ether, acetone, carbon disulfide, and benzene. Many of the solvents used in internal preparations are complex solutions in themselves, such as syrups, elixirs, and aromatic waters.

3-7. COMPOUND SOLUTIONS

In a strict pharmaceutical sense, a compound solution is one in which one substance has been made soluble by the prior solution of another substance in the solvent. For example, iodine is not soluble in water by itself. If, however, potassium iodide is first dissolved in the water and iodine is then added, it readily goes into solution. The finished product in this case is a true compound solution. There are other drugs besides this one, which are soluble only in a solution of a specific salt.

3-8. SATURATED SOLUTIONS

a. **Description**. A saturated solution is a solution--at a specified temperature--that cannot dissolve any additional solute. A solution saturated at 25º Celsius (C) will become unsaturated if the temperature rises above 25º C. At cooler temperatures, it will become supersaturated; that is, it will contain more solute than would normally dissolve at the cooler temperature. Some of the solute is likely to precipitate and make the solution cloudy. For this reason, it is best to make "saturated" solutions so that they would be saturated at about 20º C, regardless of the room temperature at the time of dispensing.

b. **Preparation of Saturated Solution of Potassium Iodide**. When the physician prescribes "saturated solution of potassium iodide" (SSKI), he is actually referring to Potassium Iodide Solution, NF. Consult the United States Pharmacopoeia/National Formulary when you need to prepare this solution.

3-9. STOCK SOLUTION

a. **Description**. Stock solutions, either purchased or prepared in advance, are solutions of known concentration used in the manufacture of other preparations and in the compounding of prescriptions. They save time and provide a convenient method for accurately measuring small amounts of drugs to be dissolved in solutions. Since they are of known concentration, a prescribed amount of the dissolved ingredient can be accurately and quickly withdrawn by measuring out the volume of stock solution containing it. The more stable and frequently prescribed agents in solutions can be prepackaged in a standard concentration in your pharmacy. When a prescription requires a certain number of milligrams (mg) of a drug in a liquid preparation, it is not necessary for you to weigh out the amount each time, but only to measure out the number of milliliters (ml) which contain the desired amount of milligrams of solute. This can then be diluted to the desired volume or mixed with the mixture being prepared.

b. **Stability**. To enhance the keeping quality of your stock solutions, make them under aseptic conditions, using distilled water that has been recently boiled and cooled. Sterilize the stock bottles (amber colored ones are preferred) and store the solutions in a cabinet or other place as free from light as is feasible. Putting the amber bottle inside a cardboard container gives additional protection.

c. **Precautions**. Some important things to remember about stock solutions are:

(1) If the stock solution is to be used in the future, it must be stable or used up before deterioration occurs.

(2) Stock solutions must be accurately labeled when they are prepared. An accurate and complete label should record the amount of active ingredient in the total volume of solution and a specific statement on the amount of ingredient per milliliter of solution. Furthermore, all stock solutions should be labeled with the date of manufacture and the date of expiration (if possible). See figure 3-1 for a sample label for a stock solution.

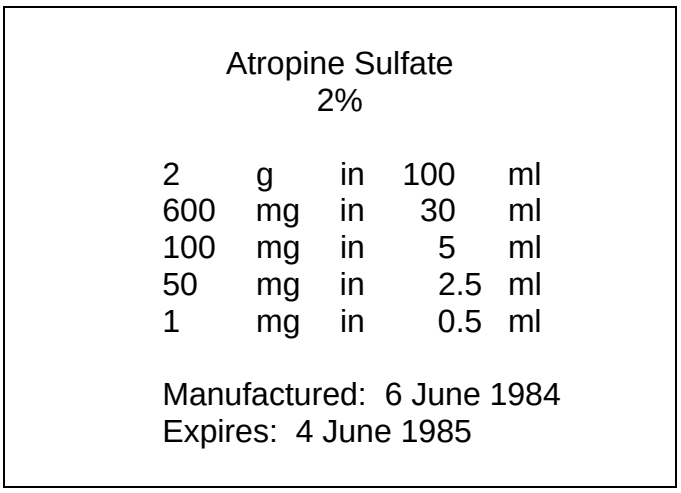


Figure 3-1. Example of label for stock solutions.

Section II. SYRUPS

3-10. INTRODUCTION

a. A syrup is defined as a sweet, concentrated, aqueous solution of a sugar in water.

b. You should remember the following facts about syrups:

(1) It is important for syrups to be "nearly saturated" because concentrated sugar solutions discourage the growth of destructive microbes while dilute solutions encourage their growth. However, if the syrup were truly saturated, some of the sugar might precipitate and ruin its appearance.

(2) The sugar most commonly used is sucrose, common table sugar, though other sugars are also used.

(3) As the definition implies, syrups are divided into two broad classes: flavoring syrups and medicinal syrups. The ultimate goal of either is to provide a palatable form in which to administer medication. Cocoa syrup (cacao syrup), orange syrup, and raspberry syrup are examples of flavoring syrups. Ipecac syrup and chloral hydrate syrup are examples of medicinal syrups. In fact, their names make it obvious to which class they belong.

3-11. PRESERVATION OF SYRUPS

In some syrup, the high quantity of sucrose is sufficient to preserve them. Others require the addition of preservatives.

a. **Temperature**. Low temperature is the best method of preserving syrups. Syrups should not be stored above 25º C (77º Fahrenheit).

b. **Glycerin**. Glycerin may be effective in preserving some syrup; especially, those made with dextrose. A 30 percent concentration is sufficient to prevent microbial growth. In addition to its preservative action, glycerin also prevents precipitation of vegetable extractives. Glycerin, although sweet, does not have the high palatability of sucrose or dextrose.

c. **Additives**. Syrups may also be preserved by small concentrations of additives such as methylparaben (0.05 to 0.25 percent), benzoic acid, or sodium benzoate.

3-12. SYRUP, USP

a. **Composition**. Syrup, USP (simple syrup) contains 850 grams of sucrose dissolved in a sufficient quantity of water to make the total volume of the preparation measure 1000 ml, thus making the syrup 85 percent weight/volume (w/v) in concentration, a concentration which is sufficient to inhibit mold growth.

b. **Properties**. Syrup, USP has a specific gravity of 1.313 (it weighs 1,313-gm per 1000-ml). It should be stored in tight containers, preferably at a temperature not exceeding 25° C. Syrup is actually bacteriocidal because it is so hypertonic that it dehydrates organisms trying to live on it before they can grow or reproduce. That is, because of its hypertonicity, fluid is withdrawn by osmosis from the microorganism until it can no longer survive.

c. **Uses**. Syrup is a sweetening vehicle and a pharmaceutical necessity for the preparation of much official and nonofficial syrup and other preparations.

3-13. OTHER SYRUPS

Some syrup is more useful in masking certain kinds of tastes than others. For example, Glycyrrhiza Syrup, USP (licorice syrup) is useful in masking salty and bitter tastes. Three of the most popular syrups for masking a variety of tastes are Cherry Syrup, USP; Raspberry Syrup, USP; and Cocoa Syrup, USP (cacao syrup).

Section III. CLASSES OF PREPARATIONS CONTAINING ALCOHOL

3-14. SPIRITS

a. **Definition**. Spirits are solutions of volatile substances in alcohol or alcohol and water. A solvent consisting of alcohol and water is said to be hydroalcoholic. The percentage concentration of volatile substances in a spirit may range from 5 to 20 percent. The active ingredient of a spirit may be solid, liquid, or gaseous.

b. **Uses**. Spirits are generally used internally for their medicinal value, by inhalation for their medicinal value, and as flavoring agents. Spirits are sometimes used in the preparation of aromatic waters and other medicinals that require flavoring.

c. **Incompatibilities**. Spirits, because of their high alcoholic content and volatile oil content, do not mix well with water or dilute alcoholic solutions. Such a dilution usually results in separation of the oil. In general, spirits should not be mixed with salt solutions because salts are often soluble in water but insoluble in alcohol and may precipitate in a hydro-alcoholic solution. Spirits should be kept in tight containers because they evaporate easily. They should also be protected from light by dark, amber-colored bottles.

3-15. TINCTURES

a. **Definition**. Tinctures are alcoholic or hydro-alcoholic solutions prepared from vegetable drugs or chemical sources. Thus, most contain extracts from plants. Unlike spirits, they are usually made from nonvolatile substances.

(1) Potent tinctures. Tinctures of potent drugs, called potent tinctures, usually are limited to only 10-gm of original substance for every 100-ml of final solution.

(2) Non-potent tinctures. Most other tinctures, the non-potent tinctures, are limited to 20-gm of original substance for every 100-ml of final solution.

(3) Fresh drug tinctures. Lemon Tincture, USP and Sweet Orange Peel Tincture, USP, fresh drug tinctures, utilize 50-gm of original substance, the outer rind of the fruit, for every 100-ml of final solution.

b. **Uses**. With the increasing use of pure drug compounds, including synthetics as well as plant drugs, there is less need for plant extracts such as tinctures. However, a number of tinctures are used to prepare other pharmaceutical products, either for their flavoring or for the medicinal value. Other tinctures are used as local anti-infectives.

c. **Incompatibilities**. Because tinctures (like the spirits) are alcoholic solutions, more than a slight dilution with aqueous or low alcoholic solutions will cause precipitation of the active ingredients. Most tinctures are acid in reaction to litmus and

have the incompatibilities of the acids. A few are alkaline. Tinctures should be stored in tight, light-resistant containers and protected from the direct rays of the sun and from excessive heat.

3-16. ELIXIRS

a. **Definition**. Elixirs are clear, sweetened, hydro-alcoholic liquids intended for oral use. They contain flavoring substances and, in some cases, active medicinal agents. The primary solvents in elixirs are alcohol and water. Sugar or other agents are added as sweeteners. Elixirs are used either as vehicles or for the effect of the drug they contain (for example, phenobarbital elixir).

b. **Characteristics**. Elixirs are clear, usually brilliantly colored medications pleasing to the eye and the palate (taste). Because of their palatability, this form of medication is often given to infants and children.

(1) Types of elixirs. There are two types of elixirs. The medicated elixirs are used for their medicinal and therapeutic effects. The nonmedicated elixirs are used as flavoring agents and vehicles.

(2) Versatility. They are easy to prepare and are stable forms of medication. Their range of application is limited only by the number of medications that can be made into elixir form. Generally, the alcohol content of elixirs, ranging from 4 percent to 40 percent, is limited to an amount sufficient to keep the medication or active principles in solution.

(3) Incompatibility. Elixirs are often incompatible with aqueous solutions and hydro-alcoholic solutions with very low alcohol content. When combined with such solutions, the elixir generally throws some of its dissolved material out of solution because its alcohol content has been reduced. On the other hand, the aqueous solution precipitates its dissolved material because its alcohol content has been increased. Of course, the incompatibilities of specific active ingredients can vary widely.

3-17. LINIMENTS

Liniments do not always contain alcohol and they are not always true solutions. However, they are frequently studied along with spirits and tinctures. Liniments are solutions or mixtures of substances in oil, alcoholic soap solutions, or emulsions. They are for external use only. They are generally applied with friction to increase circulation of blood to the area. They are also used for their counterirritant and penetrating effects. However, there are some liniments, applied without friction, which are used for their protective, coating properties.

Continue with Exercises

EXERCISES, LESSON 3

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or best completes the incomplete statement or by writing the answer in the space provided.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the group of definitions below, select the most correct definition of the term solution.

   a. A heterogeneous mixture of two or more substances.

   b. A homogeneous mixture of a solvent and water.

   c. A heterogeneous mixture of two or more unlike substances.

   d. A homogeneous mixture of two or more substances.

2. From the groups below, select the two parts of a solution.

   a. Water and drug.

   b. Solute and solvent.

   c. Oil and water.

   d. Collyria and water.

3. From the list of advantages below, select the most appropriate advantage of the use of solutions as a pharmaceutical dosage form.

   a. Solutions are sterile and free from bacteria.

   b. Solutions are clear and easy to check for purity.

   c. Solutions are easy to administer.

   d. Solutions are easy to evaluate for microbial contamination.

4. From the list of disadvantages below, select the appropriate disadvantage associated with the use of solutions.

   a. Solutions are expensive.

   b. Solutions must be dispensed in amber bottles.

   c. Inaccurate measurements may result when using inaccurate measuring instruments.

   d. Plastic storage bottles for solutions sometimes contain chemical contaminants.

5. Of the methods below, select the method used to prepare solutions.

   a. Nuclear reaction.

   b. Simple solution.

   c. Detraction.

   d. Exhumation.

6. Of the statements below, select the statement that best describes when heat should <u>not</u> be used in the preparation of a solution.

   a. When the drug in the solution would be harmed by the heat.

   b. When the solvent would not be deteriorated by the heat.

   c. When a nonvolatile liquid is in the solution.

   d. When a plastic beaker is being used to prepare the solution.

7. From the list of definitions below, select the most correct definition of the term-saturated solution.

   a. A solution that contains a certain type of fat.

   b. A solution that contains more solute than it should at a specific solution.

   c. A solution that contains all the solute it can contain at that specific temperature.

   d. A solution that is prepared at 200° C and increased to 250° C for sterilization purposes.

8. From the list of definitions, select the definition of stock solution.

   a. A solution prepared by boiling beef or chicken parts for two hours.

   b. A solution of known concentration used in the manufacture of other preparations and in the compounding of prescriptions.

   c. A solution used to prepare ophthalmic or intravenous solutions for patient use.

   d. A solution intended to be injected into animals.

9. From the list of information below, select the information that should appear on the label of stock preparations.

   a. The concentration of the solution.

   b. The name, rank, and SSN of the preparer.

   c. The name of the patient.

   d. The name of the prescriber.

10. From the group of definitions below, select the most correct definition of the term syrup.

    a. A maple-flavored sweet preparation used to mask foul-tasting medicines.

    b. A maple-flavored sweet preparation used to mask sour-tasting medicines.

    c. A sweet, concentrated, aqueous solution of sugar in water.

    d. A homogeneous mixture of sucrose and water both in low concentrations.

11. From the list of percentage concentrations below, select the percentage concentration of sucrose in Syrup, USP.

    a. 1.313 percent.

    b. 85 percent.

    c. 30 percent.

    d. 0.05 to 0.25 percent.

12. From the group of definitions below, select the most correct definition of the term spirit.

    a. A solution that mixes well with water.

    b. A solution that has a concentration of 5 to 65 percent.

    c. A solution that must be controlled because of its alcohol content.

    d. A solution of a volatile substance in alcohol or in alcohol in water.

13. From the list of definitions below, select the most correct definition of the term tincture.

    a. An alcoholic or hydro-alcoholic solution prepared from vegetable drugs or chemical sources.

    b. An alcoholic or hydro-alcoholic solution prepared from volatile oils or other chemical substances.

    c. An alcoholic or hydro-alcoholic solution prepared from a vegetable source in at least a 25 percent concentration.

    d. An alcoholic or hydro-alcoholic solution prepared from lemon peels or volatile oils.

14. From the group of statements below, select the statement that best pertains to the storage of tinctures.

    a. Tinctures should be secured because of their high alcohol content.

    b. Tinctures should be stored in plastic containers.

    c. Tinctures should be stored in tight, light-resistant containers.

    d. Tinctures should be secured in specially designed areas out of the pharmacy because of their likelihood of causing an explosion.

15. From the group of definitions below, select the most correct definition of the term elixir.

    a. A colorless, sweetened, hydro-alcoholic liquid intended for oral use.

    b. A clear, sweetened, concentrated aqueous solution of a sugar in water intended for oral use.

    c. A clear, sweetened, hydro-alcoholic liquid intended for external application to the skin.

    d. A clear, sweetened, hydro-alcoholic liquid intended for oral use.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 3

1. d (para 3-1b)
2. b (para 3-1c)
3. c (para 3-3a)
4. c (para 3-4c)
5. b (para 3-8b)
6. a (para 3-6c(1))
7. c para 3-8a)
8. b (para 3-9a)
9. a (para 3-9c(2))
10. c para 3-10a)
11. b (para 3-12a)
12. d (para 3-14a)
13. a (para 3-15a)
14. c (para 3-15c)
15. d (para 3-16a)

End of Lesson 3

LESSON ASSIGNMENT

LESSON 4	Emulsions and Suspensions.
LESSON ASSIGNMENT	Paragraphs 4-1 through 4-14.
LESSON OBJECTIVES	After completing this lesson, you should be able to:

4-1. Given a group of definitions, select the definition of the term emulsion.

4-2. Given a group of possible types of emulsions, select the two types of emulsions.

4-3. Given a description of an emulsion and a group of terms used to describe emulsions, select the term that best describes the emulsion.

4-4. Given a group of possible advantages, select the advantage of emulsions over other dosage forms.

4-5. Select the use of emulsifying agents.

4-6. Given a group of procedures, select the procedure that should be used to add an oil soluble active ingredient to an oil in water emulsion or to a water in oil emulsion.

4-7. Given a group of procedures, select the procedure that should be used to add a water soluble active ingredient to a water in oil emulsion or to an oil in water emulsion.

4-8. Given a list of auxiliary labels, select the auxiliary label that should be attached to every bottle containing an emulsion.

4-9. Given a group of definitions, select the definition of the term suspension as presented in Lesson 4.

4-10. Given a list of auxiliary labels, select the auxiliary label that should be attached to every bottle containing a suspension.

4-11. Given a group of statements, select the statement that best applies to the storage of suspensions.

4-12. Given several groups of auxiliary labels, select the group that contains the auxiliary labels required on bottles containing lotions dispensed to patients.

SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 4

EMULSIONS AND SUSPENSIONS

Section I. EMULSIONS

4-1. INTRODUCTION

At one time emulsions were frequently prepared in the pharmacy. Now, the emulsions used in medical practice are primarily prepared by pharmaceutical manufacturers. This area of the subcourse will discuss some important considerations of emulsions. Should you be required to prepare an emulsion, you should consult a reference such as Remington's Pharmaceutical Sciences.

4-2. BACKGROUND INFORMATION

a. **Definition**. An emulsion is a liquid composed of two immiscible liquids (two substances which will not mix together), such as oil and water, in which one liquid is dispersed in small globules throughout the other liquid. The world's most naturally occurring emulsion is milk.

b. **Parts of an Emulsion**. An emulsion usually consists of two distinct liquids called phases. One phase consists of tiny globules. The other phase is the liquid surrounding the globules. The globule phase may be called the inner phase, the internal phase or the dispersed phase. The surrounding liquid is called the external phase or the continuous phase. See figure 4-1, which illustrates the two phases of an emulsion.

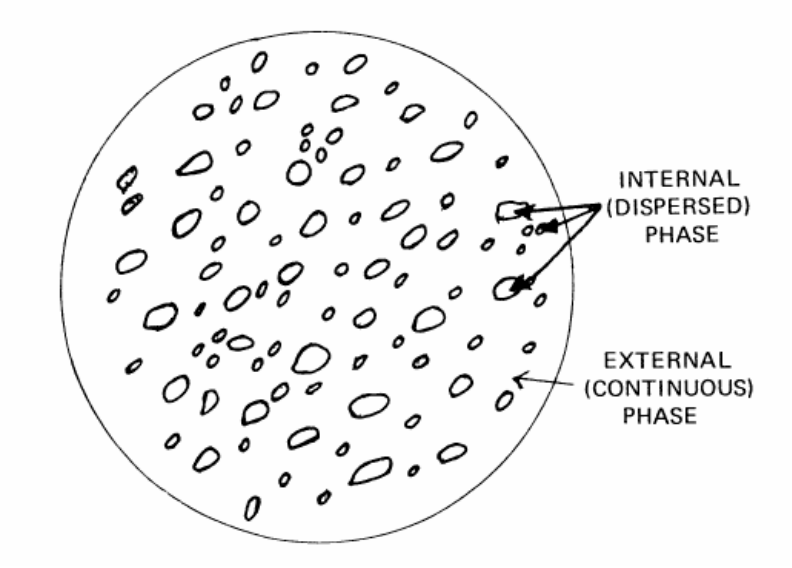


Figure 4-1. Microscopic view of the two phases of an emulsion.

c. **Types of Emulsions**. An emulsion usually consists of oil and water. When the oil is the internal phase and the water is the external phase, the emulsion is said to be an oil-in-water (o/w) emulsion. When the water is the internal phase and the oil is the external phase, it is a water-in-oil (w/o) emulsion.

d. **Creaming**. Unhomogenized milk will separate into two layers while standing. However, if it is shaken, the two layers will disappear. When an emulsion separates in this manner, we say that it has creamed. The emulsion is still good since there is no separated oil visible.

e. **Cracking**. When an emulsion separates into layers of oil and water and shaking cannot restore the original emulsion, we say that the emulsion has cracked. That is, it is no longer pharmaceutically useful as an emulsion.

4-3. THE USE OF EMULSIONS

Emulsions are used because they have some distinct advantages over other types of dosage forms. Internally, the emulsion is a satisfactory form of dosage for large quantities of unpleasant oily liquids, which cannot be given in capsules. These doses are rapidly and completely-assimilated. Thus, an oil-in-water (o/w) emulsion of cod liver oil can be prepared in which the flavored aqueous liquid surrounding the oil globules masks the greasiness and the bad taste of the oil. Externally, an emulsion can provide a homogenous ointment or lotion, which contains both oil and water soluble ingredients. Emulsions provide palatable internal preparations and uniform dosages of both internal and external preparations.

4-4. EMULSIFYING AGENTS

a. **Overview**. As you know, oil and water do not mix. Since oil and water do not mix, how is it possible to form the two phases required for an emulsion? The answer is simple--emulsifying agents.

b. **Definition**. An emulsifying agent, or emulsifier, is any substance that will promote the formation of an emulsion. The chemical structure of an emulsifying agent promotes the formation of an emulsion.

c. **Examples of Emulsifying Agents**. Acacia and tragacanth are used as emulsifying agents. For specific information on the amount of an emulsifying agent that must be used to prepare an emulsion, you should consult a reference such as Remington's Pharmaceutical Sciences.

4-5. METHODS USED TO PREPARE EMULSIONS

Emulsions are infrequently prepared in the pharmacy. Thus, this subcourse will not provide detailed instructions for the preparation of emulsions. You should be aware that several methods exist for the preparation of this dosage form. The two methods most frequently used are the continental method and the bottle method.

a. **Continental Method (4-2-1 Method)**. This is the most commonly used method for the preparation of emulsions. The common name, the 4-2-1 Method, describes the ratio of fixed oil, water, and acacia used to prepare the basic emulsion. For specific information on this method, see Remington's Pharmaceutical Sciences.

b. **Bottle Method**. This method is used to prepare small quantities of volatile oil emulsions. In this method, two parts of oil, two parts of water, and one part of powdered acacia is used. As the name implies, the basic emulsion is prepared in a bottle by vigorously shaking the components. Again, for specific information about this method, consult Remington's Pharmaceutical Sciences.

4-6. ADDITION OF OTHER INGREDIENTS TO EMULSIONS

Any number of different medicinals may be incorporated into the emulsion. It would be impossible to go into any detail in the exact procedure to take for each substance in specific situations. The following general information can be adapted to many.

a. Water-soluble ingredients are dissolved in water and added after the formation of the primary emulsion.

b. Oil-soluble ingredients are dissolved in the oil before emulsification.

c. Insoluble ingredients should be finely powdered and triturated into the product just before it is brought up to final volume.

d. It is best to add syrups and glycerin directly to the formed primary emulsion. They should not be added in large quantities.

e. Alcoholic solutions, electrolytes, and other materials which are likely to cause the emulsion to crack must be diluted to as weak a concentration as possible and added to the product just before it is brought up to its final volume.

4-7. CRACKING OF EMULSIONS

a. When an emulsion separates into its separate ingredients (when the oil and water are clearly separated and will not recombine) the emulsion is said to have "cracked" or "broken." Do not confuse a "cracked" emulsion with one that has creamed! Creaming is a natural occurrence with most emulsions and simple shaking will restore the uniformity of the preparation. However, no amount of shaking will restore the cracked emulsion to its original state.

b. The most common reason that an emulsion cracks is the addition of too much or too concentrated alcohol or electrolyte solution. Freezing will also cause an emulsion to crack.

4-8. DISPENSING AN EMULSION

a. **Container**. Emulsions of thick consistency should be dispensed in a wide-mouthed bottle or jar. The very thin emulsions may be dispensed in ordinary prescription bottles, if they will not become thicker as the emulsifier hydrates on standing. Thick emulsions cannot be conveniently poured from narrow-mouthed bottles. Clear bottles are generally preferred to amber ones, unless their contents are sensitive to light.

b. **Special Instructions.** All emulsions are damaged by excessive heat or cold. Patients should be instructed to store emulsions away from either extreme. Emulsions for internal use should be stored in the refrigerator, but they should be protected from freezing. All emulsions should bear the "Shake Well Before Using" label. Those for external use should be so labeled.

Section II. SUSPENSIONS

4-9. INTRODUCTION

Both emulsions and suspensions are types of dispersions. Suspensions are liquid preparations that contain a finely divided dispersed solid. They are quite closely related to emulsions except that their internal phase is a solid rather than another liquid. If the particle size is less than 0.1 micrometer, where a micron is a millionth of a meter, we say that we have a colloid, not a suspension. Suspensions are usually intended for external use, oral administration, or injection. The tendency of suspensions to settle out makes them slightly less desirable as a dosage form than solutions; the solid particles agglomerate and settle to the bottom, leaving the liquid phase supernatant. It is quite possible to prepare a suspension that will not settle appreciably for several months. In the pharmacy, this should be the goal for every suspension prepared: to lengthen the settling time as much as possible. The absolute minimum requirement of settling time is a rate slow enough to allow the medication to be shaken and a dose to be removed from the container that will be uniform in content each time.

4-10. SETTLING

Creaming, the separation of two liquids from one another, is characteristic of emulsions. Shaking readily disperses the creamed emulsion. Settling of suspensions is similar to this creaming, because after the settled suspension is shaken a few times it is again suitable for use.

4-11. COALESCENCE

In discussing emulsions, we described the phenomenon of cracking, in which an emulsion permanently separates into its two phases and no amount of shaking will redistribute them. The same is true of suspensions that coalesce. The particles are no longer surrounded by a coat of water or other liquid. They form into tight aggregates that do not satisfactorily redisperse in shaking.

4-12. DISPENSING SUSPENSIONS

Since all suspensions contain insoluble dispersed particles, they must be dispensed with "Shake Well Before Using" labels. Regardless of how perfect your preparation may be or how long it has stood up on the shelf without noticeable settling, sedimentation will occur eventually. When you hand the prescription to your patient, call attention to the "Shake" label and verbally repeat the "Shake" instructions so that there is not a doubt that the contents must be vigorously shaken before each dose or application is withdrawn. Point out to the patient any special storage directions. In dispensing all suspensions, instruct the patient NOT to refrigerate, except for antibiotics and others that require refrigeration. Medications subject to deterioration from light must be dispensed in amber bottles and the patient must be instructed to store them away from light. Those affected by heat should be stored away from heat, but not in a refrigerator.

4-13. MIXTURES

A mixture is an aqueous preparation containing suspended insoluble material. Mixtures too are intended for internal use. They often contain no agent to stabilize the suspension. The only official mixture is Kaolin Mixture with Pectin, NF. (The word mixture is frequently used by pharmacy personnel to refer to any aqueous preparation.)

4-14. LOTIONS

Lotions are liquid dispersions, usually suspensions, intended for EXTERNAL use. Lotions also include emulsion-like preparations such as Benzyl Benzoate Lotion, NF, which has an oil phase and an aqueous phase. Lotions tend to separate on standing and require "Shake Well Before Using" and "For External Use Only" labels. The types of medications that can be incorporated into lotions are infinite. Dermatologists prescribe a wide range of lotions for healing and cosmetic effects.

Continue with Exercises

EXERCISES, LESSON 4

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or best completes the incomplete statement or by writing the answer in the space provided.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the group of definitions below, select the most correct definition of the term emulsion.

   a. A liquid composed of two miscible liquids, such as water and syrup.

   b. A liquid composed of two immiscible liquids in which one liquid is dispersed in small globules throughout the other liquid.

   c. A liquid composed of two substances, such as a liquid and a solid, which will not mix.

   d. A liquid composed of three or more immiscible liquids in which oil and water are mixed.

2. From the group of responses below, select the response that contains the two types of emulsions.

   a. Oil in oil/water in water.

   b. Oil in oil/water in glycerin.

   c. Oil in water/water in glycerin.

   d. Oil in water/water in oil.

3. Upon seeing an emulsion, you observe that it has separated into two distinct layers. Upon shaking the bottle containing the emulsion, you observe that the original emulsion cannot be restored. Obviously, this emulsion has:

   a. Creamed.

   b. Cracked.

   c. Emulsified.

   d. Mummified.

4. From the list below, select the advantage of the use of emulsions over other pharmaceutical dosage forms.

   a. Emulsions can be used to administer oily liquids that cannot be given in capsules.

   b. Emulsions, when properly prepared, can be frozen to maintain their effectiveness indefinitely.

   c. Emulsions can easily be administered orally to comatose patients.

   d. Emulsions can be sterilized in an autoclave before being applied to burn injuries.

5. Select the purpose for the use of emulsifying agents.

   a. To promote the formation of a solution.

   b. To chemically prevent the two immiscible liquids from mixing.

   c. To promote the formulation of an emulsion.

   d. To promote a chemical reaction between the two immiscible liquids.

6. You wish to have an oil-soluble active ingredient in an oil in water emulsion. Select the best way to prepare the product.

    a. Prepare the primary emulsion and add the active ingredient later.

    b. Dissolve the active ingredient in the oil; then prepare the primary emulsion.

    c. Rapidly mix the oil, water, active ingredient, and emulsifying agent using the bottle method.

    d. Suspend the active ingredient in the water; then prepare the primary emulsion.

7. From the list of auxiliary labels below, select the label that should be attached to every bottle containing an emulsion.

    a. “Caution: This Medication May Be Habit Forming.”

    b. “Shake Well Before Using.”

    c. “For External Use Only.”

    d. “For the Eye.”

8. From the group of definitions below, select the correct definition of the term suspension.

    a. A solid preparation that contains a finely divided and dispersed solid.

    b. A liquid preparation that contains a finely divided and dispersed solid.

    c. A solid preparation that contains a finely divided liquid.

    d. A liquid preparation that consists of at least three distinct phases.

9. After shaking a suspension, you discover that the particles have formed tight aggregates that which will not satisfactorily re-disperse. What should you do?

   a. Discard the suspension.

   b. Agitate the suspension until the aggregates are broken.

   c. Place the suspension into a blender and turn the machine on.

   d. Place a “Shake Well Before Using” label on the bottle and dispense it.

10. From the group below, select the statement that best applies to the storage of suspensions.

   a. Suspensions should be frozen to extend their shelf life.

   b. Suspensions should be stored upside-down to prevent sedimentation.

   c. Antibiotic suspensions should be stored in the refrigerator.

   d. Suspensions subject to deterioration from light should be stored in clear bottles so you can see if they have deteriorated.

11. From the groups of auxiliary labels below, select the group that contains the two auxiliary labels required to be placed on bottles containing lotions that will be dispensed to patients.

   a. “For the Eye” and “Shake Well Before Using.”

   b. “Caution: This medication Can Be Habit Forming” and “For External Use Only.”

   c. “For External Use Only” and “Do Not Take on an Empty Stomach.”

   d. “For External Use Only” and “Shake Well Before Using.”

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 4

1. b (para 4-2a)
2. d (para 4-2c)
3. b (para 4-2e)
4. a (para 4-3)
5. c (paras 4-4a, b)
6. b (para 4-6b)
7. b (para 4-8b)
8. b (para 4-9)
9. a (para 4-11)
10. c (para 4-12)
11. d (para 4-14)

End of Lesson 4

LESSON ASSIGNMENT

L**ESSON 5**	Medicated Applications.
LESSON ASSIGNMENT	Paragraphs 5-1 through 5-11.
LESSON OBJECTIVES	After completing this lesson, you should be able to:

5-1. Given a group of definitions, select the definition of the term ointment as presented in Lesson 5.

5-2. Given several types of substances, select the type of substance that should be used as an ointment base.

5-3. Given a group of preparation procedures, select the procedure that should be used to prepare an ointment using the Fusion Method as discussed in Lesson 5.

5-4. Given a list of auxiliary labels, select the auxiliary label that should be placed on a container in which an ointment is dispensed.

5-5. From a group of definitions, select the definition of the term suppository.

5-6. From a list of possible uses for suppositories, select a common use of suppositories.

5-7. Given a group of statements, select the statement that best describes the relationship between the rectal and the oral dose of a medication.

5-8. Select, from a list of auxiliary labels, the auxiliary label that should be placed on a prescription bottle or box containing suppositories to be dispensed to a patient.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 5

MEDICATED APPLICATIONS

Section I. OINTMENTS, PASTES, AND CREAMS

5-1. INTRODUCTION

Ointments are semisolid preparations intended for external application that usually contain medicinal substances. Pastes, ointment-like preparations that contain a greater amount of solids, generally are thicker and do not melt when applied to the body. Creams are semisolid emulsions very much like ointments in consistency but are opaque rather than translucent. For purposes of dispensing, because the methods of preparation and packaging and labeling are so similar, we will discuss these three forms of medication together.

a. **Purpose of Ointments**. Ointments have several purposes. They act as vehicles for medicinal agents for topical application. They may protect, or act as emollients to, the skin. A few are counterirritants. Ointments are limited only by the number of medicinals that can be incorporated into them and, to some extent, by their absorption into the body.

b. **Desirable Qualities in Ointments**. Ointments, creams, and pastes must be smooth, never gritty. More trituration is necessary in preparing powders for incorporation into ointments than powders to be used in tablets or capsules. Since ointments, creams, and pastes are often applied to broken skin and may be absorbed into the body, extra measures of cleanliness must be taken in preparing them. Spatulas, ointment slabs, and all the equipment used to make ointments must be immaculate. The choice of an ointment base is of the utmost importance, and although it may be impossible for any single base to be ideal in every respect, the following are standards for which we strive:

(1) The base in no way adversely affects a wound to which it is applied.

(2) It is pharmaceutically elegant.

(3) It does not cause sensitization or irritation, either to unabraded or traumatized skin.

(4) It is prepared with relatively little difficulty.

(5) It is neutral (neither acidic nor basic).

(6) It does not dehydrate the area to which it is applied.

(7) It is nongreasy and nonstaining.

(8) It has permanency, good keeping qualities, and neither becoming rancid nor supporting microbial growth.

(9) It is compatible with a wide range of medicinal substances and with other bases with which it is likely to be mixed.

(10) It releases the incorporated medication effectively to the site of application, and if so intended, passes into or through the skin.

(11) It is washable. Unfortunately, not all ointments, creams, and pastes meet this requirement.

5-2. CLASSIFICATION OF OINTMENT BASES

Ointment bases can be classified according to composition and general characteristics. The ointment base or vehicle may or may not be therapeutically active. It may be used without active ingredients if only protection or emollient properties are desired. Ointment bases fall into one of these classes: oleaginous, absorption, emulsion, or water-soluble.

a. **Oleaginous Ointment Bases**. Oleaginous ointment bases include not only vegetable oils and animal fats, but also hydrocarbons derived from petroleum. Because of their nature, oils and fats become rancid and foul smelling on exposure to the atmosphere and to light. Preservatives and antioxidants are necessary ingredients in these bases. The hydrocarbon bases may include liquid petrolatum to lower viscosity or white wax to raise it. White Ointment, USP is a typical combination of hydrocarbons.

(1) Petrolatum (Vaseline). Petrolatum is a tasteless, odorless, yellowish, greasy solid with a melting point between 38º C and 60º C. White petrolatum is decolorized petrolatum. It is used more frequently than yellow petrolatum. Petrolatum is very stable, very compatible with most substances, and emollient to the skin. The consistency can easily be varied by the incorporation of mineral oil (liquid petrolatum) or white wax. Petrolatum-type ointment bases are more stable than vegetable- or animal-type bases. However, all of these bases are greasy. The degree to which they release the incorporated medication is questionable. They are able to absorb only very small amounts of water, unless treated with cholesterol.

(2) (Jelene (Plastibase). Jelene, a mixture of hydrocarbons in the liquid and wax ranges, has a jelly-like consistency. It is better than petrolatum in many respects. It maintains its consistency over a wide range of temperature without additives. It releases medication more reliably and provides a better appearing ointment.

(3) Silicones. Silicones, polymers of silicon and oxygen, make good ointments for protecting the skin from moisture.

(4) Summary of oleaginous bases. We can sum up the oleaginous ointment bases as follows:

(a) Properties. Not good water absorbers, insoluble in water, not washable, not greasy.

(b) Examples. Fats and fixed oils such as lard olive oil, cottonseed oil, petrolatum, white ointment, plastibase, and silicon bases.

(c) Advantages. Highly compatible; all but the fats and oils are stable; good emollients.

(d) Disadvantages. Difficult to remove from skin and clothing; uncertain as to yield of medicament.

b. **Absorption Bases**. An absorption base absorbs water or aqueous solutions of medicinals. These bases are generally anhydrous (waterless), hydrophilic (water loving) bases.

(1) Constituents. The most common absorption bases are composed of petrolatum mixed with animal sterols such as cholesterol. Aquaphor is a widely used and excellent example of an absorption base. Hydrophilic Petrolatum, USP is another.

(2) Summary of absorption bases. We can sum up the absorption bases as follows:

(a) Properties. Anhydrous; will absorb water; most are not washable.

(b) Example. Hydropholic Petrolatum, USP; aquaphor; Anhydrous Lanolin, USP.

(c) Advantages. Highly compatible; relatively stable to heat; can be used in anhydrous form or water can be added when emolliency is desired.

(d) Disadvantage. Greasy.

c. **Emulsion Bases**. Emulsion ointment bases consist of an aqueous phase, an oleaginous phase, and an emulsifying agent. They are true, solid emulsions. Emulsion bases may be either oil-in-water (o/w) or water-in-oil (w/o), usually depending upon the phase in which the emulsifier is more soluble. The water phase varies from 10 percent to 80 percent of the completed ointment base.

(1) Preparation. Emulsion bases are made by melting the greasy and oily materials together in one container and heating the water and water-soluble materials in another container. At the temperature of 75º C, they are mixed together until a smooth cream results. While the mixture is still warm and thin, it may be passed through a homogenizer to improve the appearance and quality of the base. The mixture is then stirred until it congeals.

(2) Summary of emulsion bases. We can sum up the important aspects of emulsion bases as follows:

(a) Properties. The w/o emulsion bases are insoluble in water and are not washable; the o/w emulsion bases are washable and nongreasy.

(b) Example. Lanolin, USP (w/o); Hydrophilic Ointment, USP (o/w); vanishing creams (o/w).

(c) Advantages. Washable and nongreasy if oil-in-water (o/w).

(d) Disadvantages. Subject to water loss if o/w, greasy and unwashable if water-in-oil (w/o), unless, a preservative is added, the emulsion bases are subject to mold growth.

d. **Water-Soluble Bases**. The polyethylene glycol polymers, or Carbowaxes, are of great importance in ointments. The names of the Carbowaxes include numbers that roughly indicate their average molecular weight. Carbowaxes with a molecular weight in the area of 1,000 are soft, ointment-like substances. As the molecular weight increases, they become harder and they finally become waxes. They are water-soluble, nonvolatile, and do not deteriorate or support mold growth.

(1) Formulations.

(a) The most suitable Carbowax ointment bases are formulations of heavy and light molecular-weight polyethylene glycols, such as the formula below for Polyethylene Glycol Ointment, USP:

Polyethylene Glycol 4,000	40%
Polyethylene Glycol 400	60%

(b) This base is so water-soluble that not more than 5 percent water can be added in making ointments. When greater volumes of water must be added to the ointment, the following formulation is recommended:

Polyethylene Glycol 4,000	47.5%
Polyethylene Glycol 400	47.5%
Cetyle Alcohol	5.0%

(c) Up to 20 percent of water or 5 percent of alcohol can be added to this ointment.

(2) Summary of water-soluble bases. We can sum up the important aspects of the water-soluble ointment bases as follows:

(a) Properties. Anhydrous, but will absorb water and dissolve in water; washable; nongreasy.

(b) Examples. Carbowax compounds such as the polyethylene glycol ointment already mentioned, water-soluble ointment base (a federally stock-listed item of supply procurement), and bases containing pectin, cellulose, bentonite, and gelatin.

(c) Advantages. Wide range of compatibility; do not become rancid or support microbial growth; nonirritating (to the same degree as lanolin, petrolatum, etc); adhere well to skin; easily washed off; low incidence of sensitization.

(d) Disadvantages. Sometimes undergo gradual discoloration with certain drugs. Unless cetyl alcohol is added, an aqueous solution can be added only to the extent of 5 percent.

5-3. PREPARATION OF OINTMENTS

Ointments are prepared in the pharmacy by either incorporating the active ingredient(s) into the chosen base or by melting the base and active ingredient(s) together. The two methods are presented below:

a. **Incorporation Method**.

(1) Equipment. Most ointments made in the pharmacy are prepared simple incorporation, in a mortar either with a pestle or on an ointment slab with a spatula. An ointment slab is a heavy piece of glass with a rough surface on one side to help reduce the size of solid particles.

(2) Procedure. Triturate solid ingredients in a mortar until they are very fine. Then, in a mortar or on an ointment slab, make a paste of the powder with an equal amount of base. This is called levigation. Thoroughly mix the paste with another volume of base equal to that of the paste. Then continue this routine of mixing equal amounts of paste and base until the entire base has been added and you have a uniform preparation with a very small particle size. A mortar and pestle should be used for incorporating liquids into a base or for preparing larger quantities of an ointment.

b. **Fusion Method**. The fusion method is particularly useful when solid waxes are included in the ointment to add viscosity. In this method, first melt the substance with the highest melting point by using a water bath, but use as little heat as necessary. Then add the other ingredients on the basis of their decreasing melting points. When the entire mixture is liquefied, remove it from the water bath. Then stir the mixture until it congeals, to prevent possible separation and crystallization.

5-4. DISPENSING OINTMENTS

Ointments are traditionally packaged in jars and collapsible tubes. The jars are made of glass that is either green or opaque white. Ordinary tin tubes are convenient to the patient because they are easier to carry and do not break when they are dropped. They are especially valuable for ointments that lose moisture or decompose on exposure to the atmosphere.

a. **Filling Ointment Jars**. Ointment jars, available in many sizes ranging from 1/4 ounce to a pound and larger, may be filled by packing the ointment into them with a small spatula. In packing, the sides and bottom all the way around should be covered first, adding the final portions to the center and top in order to minimize air pockets. Melted ointments containing no material likely to settle out may be poured into containers while still warm and fluid. In either case, the ointment should be smoothed off at the top before the lid is closed.

b. **Filling Ointment Tubes**. You can fill ointment tubes at the pharmacy by first rolling the ointment into a glassine powder paper to make a cylinder just smaller than the base of the tube. Remove the cap of the tube so that air will not be trapped when the ointment is inserted. Insert the roll, ointment and paper combined, as far into the tube as the roll will go and close it by carefully flattening the end of the tube. Hold the end of the tube closed with firm pressure from the side of a spatula and carefully pull the glassine paper out of the tube. The ointment is left in the tube. Fold the end of the tube over twice, crease it tightly, and score it several times with the spatula edge to prevent it from opening during use.

c. **Labeling**. Select a label corresponding in size to the size of the jar being used. Metal ointment tubes should be moistened with tincture of benzoin before the label is applied to help the label adhere. When the label has been put into place, it should be covered with a strip of cellophane tape. The auxiliary label "For External Use Only" is required on all ointments, pastes, and creams.

Section II. SUPPOSITORIES

5-5. INTRODUCTION

Suppositories are solid bodies of various weights and shapes, adapted for introduction into different orifices of the human body, usually the rectum or vagina. Suppositories usually dissolve, melt, or soften at body temperature.

5-6. SHAPES AND WEIGHTS

The shapes and weights of suppositories depend on the route of administration. See figure 5-1 for the various shapes that a suppository may take.

a. **Rectal Suppositories**. The most suitable shape for rectal suppositories is that of a bullet tapered on one or both ends with the base longer and more tapered than the head. This shape allows easy insertion and helps prevent accidental expulsion of the suppository before it has the time to melt. Rectal suppositories weigh about 2 grams. Suppositories for children should be smaller, longer, and narrower than adult suppositories.

b. **Vaginal Suppositories**. Vaginal suppositories should weigh about 5 grams.

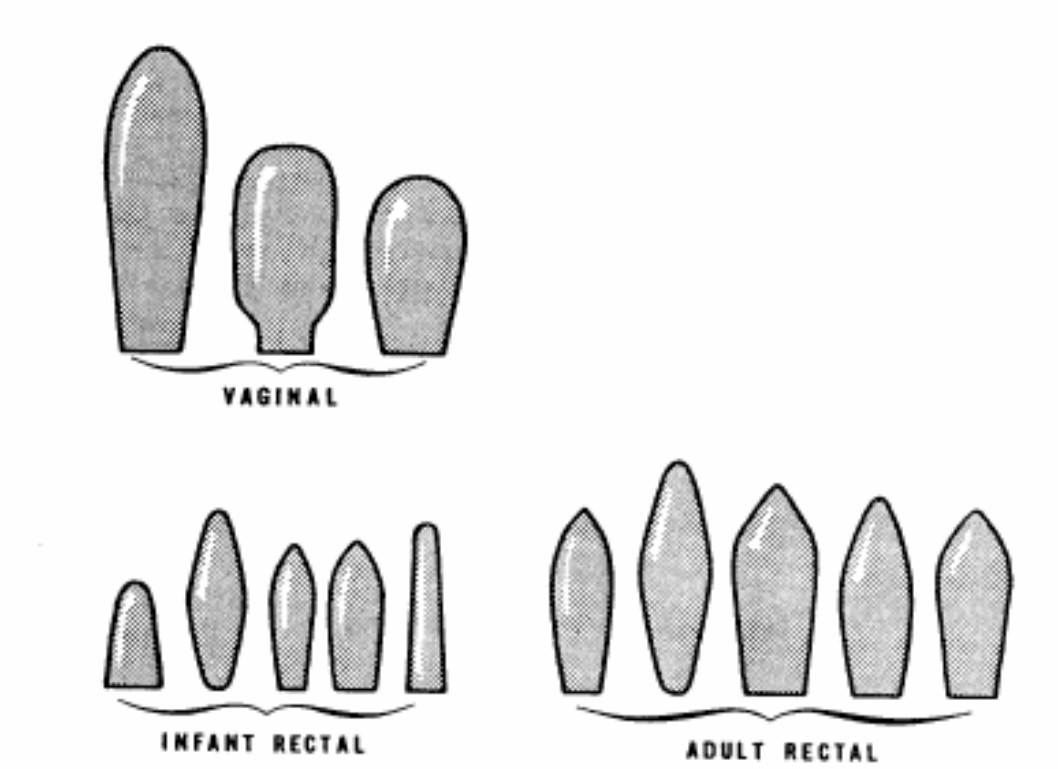


Figure 5-1. Identification of suppositories.

5-7. ACTION

Suppositories have a local effect or a systemic effect (an effect on the entire body), depending upon the active ingredients in the suppository.

a. **Local**. Frequently, a local action is desirable for a rectal or vaginal inflammation or condition. In such cases, the local action of an emollient, local anesthetic, astringent, analgesic, or antibiotic is sought. Drugs that are not absorbed from the site to which they are introduced can exert only a local effect. Those that are absorbed may exert both a local and a systemic action. The concentration of the agent will have a bearing upon the systemic action, if the drug is absorbable.

b. **Systemic**. The systemic actions for which suppositories are used are limited only by the drug's solubility and absorbability. Thus, it is possible to administer antiemetics, antibiotics, analgesics, antipyretics, muscle relaxants, sedatives, hypnotics, and so on, in the form of suppositories.

5-8. USES OF SUPPOSITORIES

Suppositories are often used when the patient is unable to swallow medications. For example, a patient who is vomiting would probably be unable to swallow (and retain) a tablet or capsule. Suppositories can be used as vehicles for antiemetics (drugs which prevent nausea and vomiting) and sedatives. Further, suppositories can be used as vehicles to carry drugs that irritate or upset the stomach.

5-9. DOSES

Extensive testing and research have shown that, because of many variables, there is no accurate relationship of rectal to oral dose. That is, it cannot be said that half, twice, or four times the oral dose is necessary to elicit the same response rectally. In practice, however, the rectal dose prescribed is normally in the range between one-half and twice the oral dose. Factors entering this variable dose are: the nature of the base used, rapidity of release of the active principles, the nature of the active medication, and the solubility and absorbability of the drug. The inability to accurately calculate a rectal dose for medication is probably the biggest reason that more and more drugs are not routinely given by the rectal route.

5-10. SUPPOSITORY CASES

a. **Theobroma Oil**. Theobroma oil (cocoa butter) is a yellowish-white, greasy-to-the-touch, nonirritating, emollient substance with the characteristic odor of chocolate. It is solid at room temperature and begins to liquefy at about 30º C (94º Fahrenheit (F)). Thus, at body temperature (37º C/98.6º F), theobroma oil is a liquid.

(1) Effect of excessive heat. Cocoa butter has a crystalline structure which breaks down when overheated. If suppositories are made from overheated cocoa butter, they will liquefy at approximately 23º to 24º C (75º F) rather than the desired higher temperature of 30º C (94º F). Therefore, when making suppositories of theobroma oil, always be careful to use only enough heat to liquefy the material, NEVER enough to destroy the natural crystalline structure.

(2) Raised or lowered melting point. When substances such as chloral hydrate and liquefied phenol are added to theobroma oil, they cause the melting point of the finished suppository to be greatly lowered. They may become soft or even liquid at room temperature. In addition, unusually warm or cold climates make the melting point of cocoa butter suppositories unsatisfactory.

b. **Glycerinated Gelatin**.

(1) There are many different formulas for this substance. They involve varying amounts of glycerin, gelatin, and water. The following formula for making pure or medicated glycerinated gelatin suppositories has been recommended.

Medicinal substance (prescribed quantity)
Purified water, a sufficient quantity to make .. ... 10 g
Gelatin, granular …….……. 20 g
Glycerin .....……..... 70 g

(2) Unlike cocoa butter suppositories, glycerinated gelatin suppositories do not melt at body temperature. Instead, they dissolve in body secretions or in contents of the cavity into which they are introduced. The time necessary for solution varies, depending upon the ratio of the ingredients, and the presence of peptizing agents or chemicals.

c. **Polyethylene Glycols**. These substances are solid at room temperature and very soluble in water. Suppositories made with polyethylene glycol bases must be prepared by the fusion method. They are popularly called Carbowaxes and the increasing solidity is identified by an increasing number in the name. Carbowax 300 is a viscid liquid; Carbowax 1540 is a solid. The Carbowaxes are becoming ever more popular as suppository bases and are excellent for water-soluble medicaments. Other water miscible formulations are surface active derivatives of polyethylene glycol and they are nonionic. An example is polyethylene glycol sorbitan monopalmitate (Tween 61).

5-11. DISPENSING

a. **Packaging**. Glycerin and glycerinated gelatin based suppositories are best dispensed in tightly closed, glass bottles with wide mouths. They are hygroscopic (readily absorb and retain moisture) and unless protected from the atmosphere will absorb water. Cocoa butter and Carbowax based suppositories may be dispensed in cardboard boxes containing partitions so that each suppository has its own compartment. If the suppository is wrapped individually in foil, the need for compartments is removed and such suppositories can be correctly dispensed in plain boxes. Suppositories containing volatile ingredients such as menthol and liquefied phenol should be dispensed in wide-mouthed, tightly closed, glass bottles.

b. **Labeling**. Directions on the label should specify use of the suppositories and their site of insertion. A "Keep in Cool Place" or “Refrigerate" label should be used. The patient should be instructed to remove the foil wrapping before insertion of the suppository.

Continue with Exercises

EXERCISES, LESSON 5

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or best completes the incomplete statement or by writing the answer in the space provided.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the group of definitions below, select the most correct definition of the term ointment.

   a. A semi-solid preparation intended for oral use.

   b. A semi-solid preparation that is thicker than a paste.

   c. A semi-solid preparation that can be sterilized by filtration.

   d. A semi-solid preparation intended for external application.

2. From the list below, select the type of substance that can be used as an ointment base.

   a. Adsorption.

   b. Lotion.

   c. Emulsion.

   d. Emollient.

3. When using the Fusion Method (melting base and active ingredients together), the different parts of the ointment should be melted separately. Select the statement that best describes the preparation procedure.

    a. The substance with the lowest melting point should be melted first.

    b. The substance with the highest melting point should be melted first.

    c. The substance with the highest melting point should be melted last.

    d. After all the ingredients have been melted, the liquid ingredients should be removed from the heat and placed in a refrigerator to cool. Do not stir the liquid.

4. From the list below, select the type of auxiliary label that should be placed on a container in which an ointment is dispensed.

    a. “Refrigerate--Do Not Freeze.”

    b. “Shake Well.”

    c. “For The Eye.”

    d. “For External Use Only.”

5. From the group of definitions below, select the most correct definition of the term suppository.

    a. Semi-solid bodies of various weights and shapes adapted for introduction into different orifices of the human body.

    b. Solid bodies of various weights and shapes adapted for oral use.

    c. Solid bodies of various weights and shapes adapted for introduction into different orifices of the human body.

    d. Semi-solid dosage forms intended for introduction into the rectum or vagina.

6. From the list of uses below, select a common use of suppositories.

   a. As a vehicle for an emetic.

   b. As a vehicle for an anti-emetic.

   c. As a vehicle for an anti-diarrheal.

   d. As a vehicle for an anthelmintic.

7. From the group of statements below, select the most correct statement pertaining to the relationship between the rectal and oral dose of a medication.

   a. The oral dose of a medication should be approximately one-half of the rectal dose.

   b. The rectal dose of a medication should be approximately twice that of the oral dose.

   c. The rectal dose of a medication should be approximately three times that of the oral dose.

   d. There is no known accurate relationship between the rectal and oral dose.

8. Select, from the list below, the auxiliary label that should be placed on a prescription bottle or box that contains suppositories.

   a. “Keep in a Cool Place.”

   b. “Shake Well Before Using.”

   c. “Freeze Prior To Use.”

   d. “Caution: This Medication May Be Habit-Forming.”

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 5

1. d (para 5-1)
2. c (para 5-2)
3. b (para 5-3b)
4. d (para 5-4c)
5. c (para 5-5)
6. b (para 5-8)
7. d (para 5-9)
8. a (para 5-11b)

End of Lesson 5

LESSON ASSIGNMENT

LESSON 6 Solid Dosage Forms.

LESSON ASSIGNMENT Paragraphs 6-1 through 6-15.

LESSON OBJECTIVES After completing this lesson, you should be able to:

6-1. From a group of statements, select the advantage of the capsule as a dosage form.

6-2. Given a list of numbers corresponding to the sizes of capsules, select the number that corresponds to the largest size capsule.

6-3. Given a group of procedures, select the procedure to be followed when dispensing capsules.

6-4. Given a group of definitions, select the definition of the term tablet.

6-5. From a group of statements, select the advantage associated with the tablet as a dosage form.

6-6. Given a group of statements, select the disadvantage associated with the tablet as a dosage form.

6-7. Given a list of substances and/or types of substances, select the substance and/or type of substance that is often a component of tablets.

6-8. Given a group of definitions and the name of a particular type of tablet (that is, chewable tablet), select the definition of the given type of tablet.

6-9. Given a group of uses and the name of a particular type of tablet (that is, chewable tablet), select the use of the given type of tablet.

6-10. Given a group of statements, select the statement associated with the dispensing of tablets.

6-1l. From a group of definitions, select the most appropriate definition of sustained-release dosage form.

6-12. Given a group of graphs, select the graph that best illustrates the blood level of medication obtained by the administration of a sustained-release dosage form.

6-13. From a group of methods, select the means by that a tablet dosage form can be made into a sustained-release form.

SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 6

SOLID DOSAGE FORMS

Section I. CAPSULES

6-1. INTRODUCTION TO CAPSULES

a. Capsules are one of the leading dosage forms. Countless capsules are dispensed to patients every day. Perhaps you have taken some capsules during the past year. If you have, you are already aware of some of the advantages and disadvantages of this dosage form.

b. A capsule is a gelatin or methylcellulose shell designed to hold solids and liquids for oral administration. Capsules are of two varieties. The hard capsule is intended to contain solids, while the elastic (soft) capsule is designed to hold liquids.

6-2. ADVANTAGES OF CAPSULES

Capsules have advantages over other dosage forms. Some of these advantages are:

a. Capsules effectively mask the odor and taste of substances.

b. Capsules are a professional looking, uniform, clean, and elegant dosage form.

c. Capsules provide a rapid release of medication in the stomach because of their rapid disintegration.

d. Capsules provide accurate dosage.

6-3. SIZES OF CAPSULES

Figure 6-1 shows the actual sizes of some capsules and the relative amounts of aspirin each will hold.

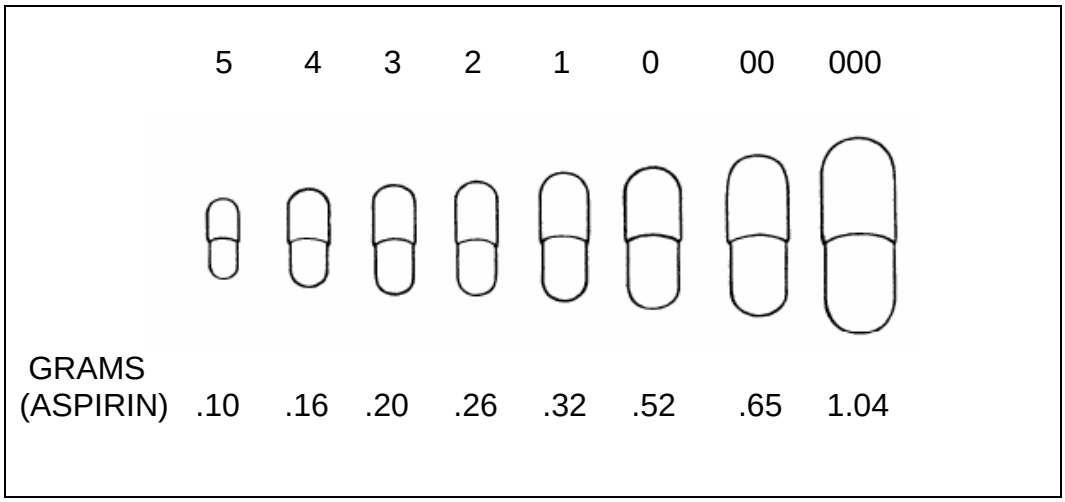


Figure 6-1. Sizes of hard capsules.

6-4. STORING AND DISPENSING

a. **Storing**. Gelatin capsules become brittle when they are stored at low humidity and they become soft, sticky, or liquid at high humidity. Consequently, empty gelatin capsules, as well as filled ones should be stored in a cool, dry place in tight containers.

b. **Dispensing**. Capsules should be dispensed in glass or plastic containers that protect them from moisture and dust. Capsules that are adversely affected by the atmosphere should be in a tightly closed container and the patient should be instructed to keep the bottle tightly closed except when withdrawing a dose.

Section II. PILLS AND TABLETS

6-5. PILLS

a. The word "pill" is probably one of the most misused words in pharmacy. Invariably, a person will call a tablet, a capsule, or any other shaped solid medication for oral administration a "pill." To many people, a pill is not a particular class of medication, but rather many different- looking, variously shaped and sized little things that are to be swallowed, dissolved in water, retained in the mouth, or chewed and swallowed. Therefore, you should know what a pill really is. A pill is a spherical or oval form of oral medication. It is made by incorporating a medication into a plastic or pliable mass, rolling out this mass into a long pipe, cutting it into the specified number of pieces, and rolling these pieces between the fingers or in a pill machine until they are globular. A pill should be distinguished from tablets, capsules, and other forms of medication.

b. Less than a century ago, the vast majority of the prescriptions filled were for pills. Due to the advent of more easily prepared, cheaper, and more efficacious dosage forms, pills are rarely prepared in pharmacies now and constitute only a very small fraction of the commercially prepared medications.

6-6. TABLETS

a. The tablet is a widely used dosage form. Tablets are supplied in many shapes, sizes, and colors.

b. A tablet is a solid medicated dosage form made by compression or molding.

6-7. ADVANTAGES OF TABLETS

a. **Precision of Dosage**. Suppose you select a bottle of 250 aspirin tablets which has a label statement that each tablet contains 325-milligrams (mg) of aspirin. How can you be confident that each tablet contains 325-mg of aspirin? The United States Pharmacopoeia/National Formulary is specific in stating standards for tablets. Thus, when a physician prescribes two tablets of aspirin (325-mg per tablet), the patient will receive 650-mg of drug. Liquid preparations are difficult to measure accurately (for example, one teaspoon might contain 5-milliliters (ml), while another teaspoon might contain 4-ml).

b. **Prolonged Stability**. Some drugs are more stable in tablet form than in solution or suspension form. Hence, supplying the medication in tablet form ensures that the drug will have an acceptable stability period. Of course, the expiration date of any medication should be checked before that medication is dispensed.

c. **Ease of Handling**. Tablets are easy to count and dispense. They are also easy for the patient to obtain from the container for administration purposes.

d. **Ease of Storage**. Tablets come supplied in a wide-variety of container sizes. The containers are easy to store. Many tablets are now supplied in plastic containers.

6-8. DISADVANTAGES OF TABLETS

Although tablets are widely used, they do have some disadvantages. The following are two disadvantages of tablets:

a. **Predictability of Absorption**. It is sometimes difficult to predict the actual amount of active ingredient that will be absorbed into the patient's bloodstream. For example, if a tablet fails to disintegrate properly in the patient's gastrointestinal tract, the patient cannot receive the therapeutic dose of the drug the prescriber desired.

b. **Inability of the Patient to Swallow**. Very young or elderly patients may be unable to swallow tablets. In this situation, another dosage form should be prescribed.

6-9. COMPONENTS OF A TABLET

You closely observe two tablets that are the same size. One tablet is labeled 325 mg while the other tablet is labeled 500 mg. How can this be since they are the same size? Tablets contain ingredients other than the active ingredient as stated on the drug container label. Most tablets contain at least five ingredients. Other tablets contain additional ingredients (for example, sweeteners and coloring agents). The following five components are often found in tablets:

a. **Active Ingredient**. The active ingredient is the chemical substance that is to produce a desired pharmacological effect in the patient.

b. **Binder**. The binder is the substance that holds the tablet together.

c. **Diluent**. The diluent is the "filler" that provides the desired extra volume for the tablet. For example, imagine a tablet that is labeled 2-mg. Actually, the tablet might weigh 175 mg. Does this mean the manufacturer made a mistake and put too much active ingredient in the tablet? Probably not. Much of this extra weight is diluent.

d. **Lubricant.** A lubricant is a substance that serves two functions. First, the lubricant prevents wear and tear on the tablet-making machine. Second, it makes it easier for the tablet to be removed from the tablet-forming mold.

e. **Disintegrant**. A disintegrant helps the tablet break apart and dissolve in the patient's gastrointestinal tract. Many disintegrants act by absorbing water and splitting the tablet into many small pieces.

6-10. TYPES OF TABLETS

Many types of tablets exist. Tablets are frequently categorized based upon their use.

a. **Common Oral Tablets.**

(1) Definition. An oral tablet is a solid medicated dosage form made by compression or molding and intended to be swallowed whole.

(2) Use. The oral tablet is used when the patient is able to swallow and the drug is not hindered by gastric juices.

b. **Chewable Tablets**.

(1) Definition. A chewable tablet is a tablet meant to be chewed before swallowing.

(2) Use. The chewable tablet is used when the patient cannot swallow a whole tablet. Further, the chewable tablet is used whenever the tablet needs to be broken down before entering the patient's stomach. Chewable children's vitamins are frequently seen advertised.

c. **Enteric-Coated Tablets**.

(1) Definition. An enteric-coated tablet is a tablet that has a special outer covering designed to dissolve in the small intestine. Once the enteric-coating is dissolved, the tablet disintegrates and the active ingredient can be absorbed by the patient.

(2) Use. Enteric-coated tablets are used when the active ingredient is destroyed by substances in the stomach. In addition, enteric-coated tablets are indicated when the stomach is irritated by the drug in the tablet.

d. **Buccal Tablets**.

(1) Definition. A buccal tablet is designed to be dissolved in the mouth between the cheek and gum.

(2) Use. Buccal tablets are used when the drug is unstable in the stomach or when a rapid onset of drug action is desired.

e. **Sublingual Tablets**.

(1) Definition. A sublingual tablet is dissolved in the mouth under the tongue.

(2) Use. Sublingual tablets are used when the drug is unstable in the stomach or when a rapid onset of drug action is desired. For example, nitroglycerin tablets are placed under the tongue by patients who are having certain types of cardiac (heart) difficulties.

f. **Effervescent Tablets**.

(1) Definition. Effervescent tablets are dissolved in water with a subsequent release of carbon dioxide. Effervescent tablets should always be dissolved in water since patients who swallow the tablets whole can experience certain gastrointestinal difficulties.

(2) Use. Effervescent tablets are easily placed in solution for a patient to drink. The patient absorbs the drug more rapidly because the active ingredient is in solution.

g. **Extended Action Tablets.**

(1) Definition. An extended action tablet releases its medication over a prolonged period of time.

(2) Use. Since the active ingredient is released over a prolonged period, the drug is able to produce its actions over a long period.

h. **Lozenge**.

(1) Definition. A lozenge is a tablet designed to be slowly dissolved in the mouth or upper throat.

(2) Use. Lozenges are used for their local action. Many over-the-counter "sore throat" medications are supplied in lozenge form.

6-11. DISPENSING TABLETS

a. Tablets should not be touched by the hands during the process of filling the prescription.

b. Tablets should be dispensed in glass or plastic vials. A container with a tight seal will help protect the tablets from moisture. A child-resistant container should be used to contain the dispensed tablets.

Section III. SUSTAINED-RELEASE DOSAGE FORMS

6-12. INTRODUCTION TO SUSTAINED-RELEASE DOSAGE FORMS

A sustained-release dosage form is designed to maintain constant levels of a drug in the patient's bloodstream by releasing the drug over an extended period. Maintaining constant blood levels of the drug in the bloodstream increases the therapeutic effectiveness of the drug.

6-13. ADVANTAGES

One advantage of sustained-release dosage forms is that medication must be administered less often than other dosage forms. Another advantage is that it reduces fluctuations of drug concentration in the blood. (See figures 6-2 and 6-3 for a graphic illustration of this principle.) Thus, the patient is not repeatedly subjected to amounts of the drug which are less than adequate or more than adequate. Nor does the blood chemistry undergo repeated chemical imbalances, which might be detrimental to the patient's health.

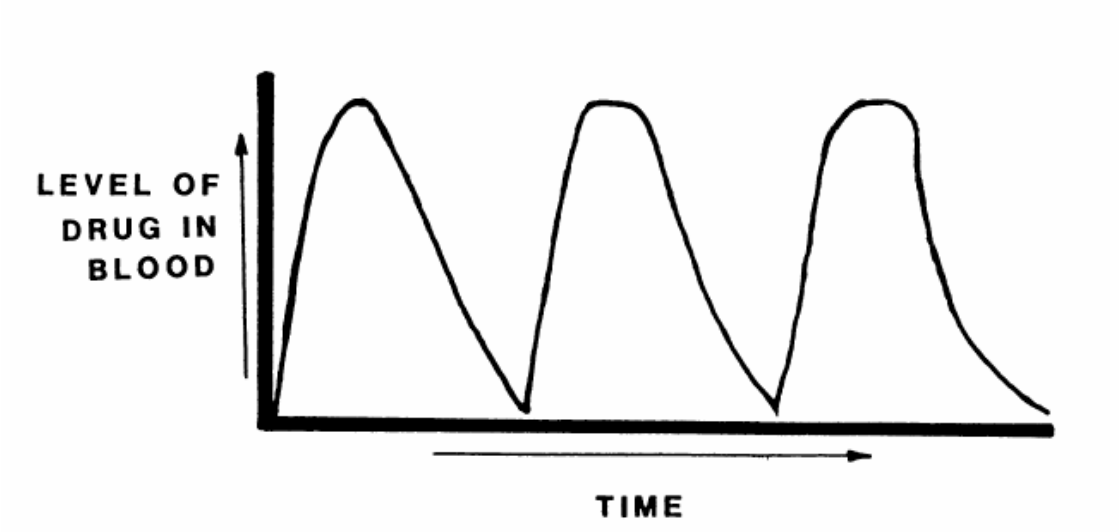


Figure 6-2. Effect of divided doses in blood.

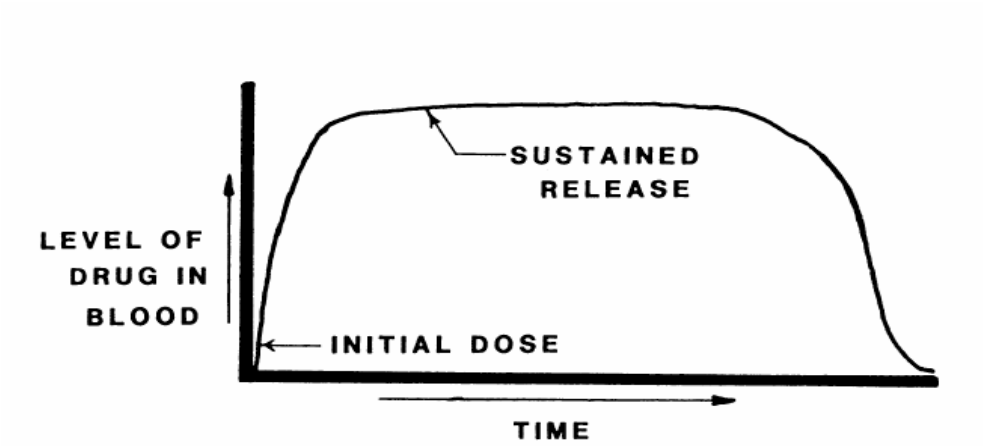


Figure 6-3. Effect of sustained-release dosage form in blood.

6-14. DISADVANTAGES

There are several disadvantages and limitations of this form of dosage. Sustained-release dosage forms are more expensive to produce. Variation of the size of the dose for a particular individual is difficult or impractical. Once the medication has been administered, it cannot be discontinued until its effects have finally ceased. In addition, some drugs are not suitable for preparation in this form.

6-15. MODES OF OPERATION

The initial dose of sustained-release medication provides sufficient drug at the time it is administered to produce the desired therapeutic effect. Thereafter, as the drug is removed from the body, more drugs, the sustained-release, must be supplied to keep a constant level in the blood. There are various means of achieving this.

a. **Capsules**. The original medication in this category is a capsule containing a number of small pellets. A full and immediate dose is provided to the bloodstream from these capsules by uncoated pellets that dissolve quickly. Other pellets, coated with varying thicknesses of a slowly soluble aterial, supply the bloodstream with enough drug to keep the concentration at the desired level. In addition, ion exchange resins have been used in some sustained-release capsules to release drugs at the proper intervals.

b. **Tablets**. In addition to capsules, some tablets provide sustained release.

(1) Granules. Some sustained-release tablets are made by compressing granules with varying coats into a tablet. The coats dissolve at different times, much like those in the capsules discussed above.

(2) Slowly soluble core. Some tablets are manufactured with an outer coating that dissolves quickly to give the initial dose. The core of this tablet, consisting of a slowly soluble base containing additional drug provides the sustained release. It is possible to achieve the same effect with layered tablets, which are often flat and cylindrical to give a constant sustained dose.

(3) Insoluble matrix. This tablet is an insoluble network of channels containing the drug. Enough of the drug is immediately extracted from the outer channels to provide the initial dose. Thereafter, the drug is extracted from the inner channels of the tablet less rapidly, producing the sustained release.

(4) Ion exchange resins. Ion exchange resins are sometimes used in tablets to provide sustained release.

(5) Repeat-action tablets. Repeat-action tablets are not really sustained-release tablets. They consist of an outer layer that dissolves quickly and provides the initial dose. Within is another tablet with a special coating that dissolves in about four hours and releases another full dosage. It is useful in avoiding the necessity of waking in the middle of the night to take a second tablet.

Continue with Exercises

EXERCISES, LESSON 6

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or best completes the incomplete statement or by writing the answer in the space provided.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the group of statements below, select the appropriate advantage of the capsule as a dosage form.

   a. Capsules can be made opaque so light cannot penetrate the shell and decompose the drug.

   b. Capsules can mask the odor and taste of a drug.

   c. Capsules can be handled with the fingers without harming the shell.

   d. Capsules can be easily and quickly prepared without the use of pharmacy equipment (that is, mortar and pestle, pharmaceutical balance, and so forth).

2. From the list of capsule sizes below, select the number that represents the largest size capsule.

   a. 0.

   b. 1.

   c. 3.

   d. 5.

3. Select the statement that best describes a procedure to be followed when dispensing capsules.

    a. Capsules should be dispensed in paper boxes so the capsules will not stick together.

    b. Capsules can be dispensed in any type of container since they are not readily affected by atmospheric conditions.

    c. Capsules should be dispensed in glass or plastic containers that can be tightly closed.

    d. Capsules can be handled with the fingers while counting for dispensing.

4. From the group of definitions below, select the most appropriate definition of the term tablet.

    a. A spherical or oval form of oral medication made by incorporating a medication into a plastic or a pliable mass, rolling the mass into a long pipe, cutting the pipe into appropriate size pieces, and rolling the pieces into globular shapes.

    b. A solid medicated dosage form made by compression or molding.

    c. A solid dosage form prepared using soft or hard capsule shells.

    d. A type of oral medication designed to disintegrate in the small intestine to avoid gastric irritation.

5. From the group of statements below, select the advantage associated with the tablet dosage form.

    a. Tablets can be made in a variety of colors and sizes to please patients.

    b. Tablets can be handled with the fingers since they are not required to be sterile.

    c. Tablets can be quickly and easily broken to prepare intravenous injections.

    d. Tablets are precise in terms of delivering a desired dose to a patient.

6. From the group of statements below, select the disadvantage associated with the tablet dosage form.

    a. Tablets are prepared in so many shapes, colors, and sizes that it is hard to remember exactly which tablet contains a particular drug.

    b. Tablets are difficult for some patients to swallow.

    c. Tablets must be dispensed in plastic containers since they are prone to breakage in glass bottles.

    d. Tablets, especially the small ones, are difficult to accurately count since they tend to roll so easily.

7. From the list below, select the substance that is often a component of a tablet.

    a. Disinfectant.

    b. Carbon dioxide (in effervescent tablets only).

    c. Sodium chloride.

    d. Binder.

8. From the group of definitions below, select the most correct definition of an enteric-coated tablet.

    a. A tablet that has a special outer covering designed to dissolve in the small intestine.

    b. A tablet that has a special outer covering designed to dissolve in the enteric mesentery.

    c. A tablet that has a special active ingredient designed to dissolve in the small intestine.

    d. A tablet that has a special binder that protects the tablet from disintegration until it reaches the upper portion of the esophagus.

9. From the group below, select the statement that best defines the term buccal tablet.

    a. A tablet designed to be dissolved in the mouth under the tongue.

    b. A tablet designed to be dissolved in the mouth between the cheek and gum.

    c. A tablet designed to be dissolved in water before administration of the drug.

    d. A tablet designed for its slow and steady release of medication.

10. From the group of statements below, select the most appropriate statement associated with the dispensing of tablets.

    a. Tablets should be dispensed in plastic vials since the tablets are prone to breakage in glass bottles.

    b. Tablets should be dispensed in containers that contain some moisture so the tablets will disintegrate faster in the patient's stomach.

    c. Tablets should be dispensed in childproof containers.

    d. Tablets should be dispensed in see-through containers so the patient can see the type of medication inside the bottle.

11. From the definitions below, select the most appropriate definition of the term–sustained release dosage form.

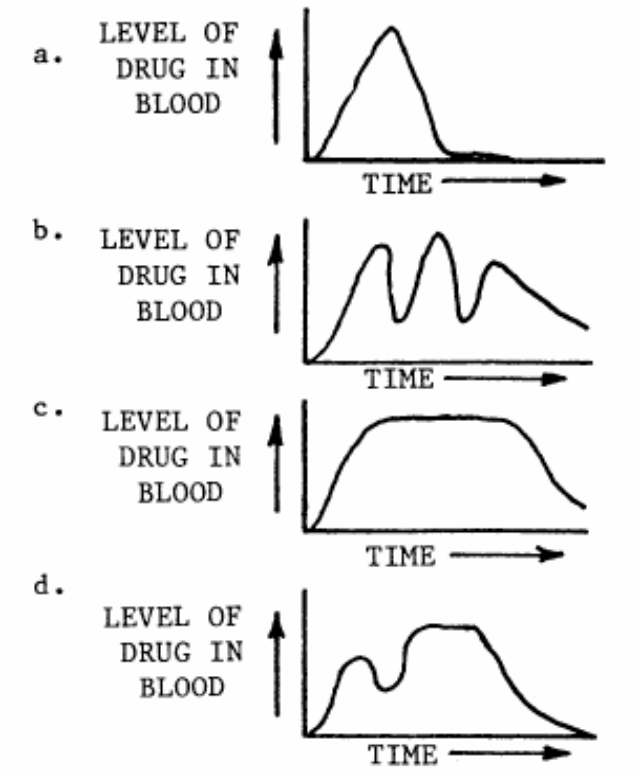
    a. A dosage form designed to maintain therapeutic effectiveness of a drug at a constant level over an extended period of time.

    b. A dosage form designed to rapidly disintegrate upon entrance into the patient's stomach.

    c. A dosage form designed to be used to relieve the symptoms of the common cold.

    d. A dosage form used to slowly disintegrate so that most of the active ingredient is released in the large intestine.

12. From the graphs below, select the graph that best illustrates the blood level of a medication given in a sustained-release dosage form.



13. From the methods below, select the means by which a tablet dosage form can be made into a sustained-release form.

    a. Granules.

    b. Small pellets.

    c. Scoring.

    d. Soluble matrix.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 6

1. b (para 6-1a)
2. a (para 6-3)
3. c (para 6-5b)
4. b (para 6-6b)
5. d (para 6-7a)
6. b (para 6-8b)
7. d (para 6-9b)
8. a (para 6-10c(1))
9. b (para 6-10d(1))
10. c (para 6-11b)
11. a (para 6-12)
12. c (para 6-3)
13. a (para 6-14b(1))

End of Lesson 6

LESSON ASSIGNMENT

LESSON 7	Ophthalmic Preparations.
LESSON ASSIGNMENT	Paragraphs 7-1 through 7-6.
LESSON OBJECTIVES	After completing this lesson, you should be able to:

7-1. Given a group of definitions, select the definition of ophthalmic preparation.

7-2. From a list of dosage forms, select the dosage form commonly used for ophthalmic preparations.

7-3. From a list of characteristics, select the characteristic required of ophthalmic solutions.

7-4. From a list of characteristics, select the characteristic required of ophthalmic suspensions.

7-5. From a list of characteristics, select the characteristic required of ophthalmic ointments.

7-6. Given a group of considerations, select the consideration involved with the preparation of ophthalmic solutions.

7-7. Given a group of patient information statements, select the statement that contains the information the patient should be told when an ophthalmic ointment is being dispensed.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 7

OPTHALMIC PREPARATIONS

7-1. INTRODUCTION

Many ophthalmic preparations are used in the practice of medicine. You probably know solutions, suspensions, and ointments are commonly used as ophthalmic products. Most ophthalmic products are no longer prepared in the pharmacy. However, you should be familiar with some of the characteristics of these important products.

7-2. DEFINITION OF OPHTHALMIC PREPARATIONS

Ophthalmic preparations are sterile products that are intended to be applied to the eyelids or placed in the space between the eyelids and the eyeball.

7-3. TYPES OF OPHTHALMIC PREPARATIONS

Three types of ophthalmic preparations are commonly encountered in the pharmacy. Each type of preparation has its advantages and disadvantages.

a. **Solutions**. Ophthalmic solutions are rather easily placed into the eye. However, care must be taken to ensure the solution remains in the eye in order to produce the desired therapeutic effect. Ophthalmic solutions usually do not impair or interfere with the vision of the patient.

b. **Suspensions**. Ophthalmic suspensions are also easily placed into the eye. In general, suspensions produce a longer effect than do solutions. Suspensions do have one disadvantage; it is difficult to ensure that the suspension does not contain particles large enough to produce eye irritation.

c. **Ointments**. Ophthalmic ointments (for example, certain antibiotic ointments) are commonly used. They are relatively easy to apply (except in the eyes of children). Ophthalmic ointments remain in contact with the eye tissues for an extended period. Hence, they usually produce a therapeutic effect of long duration. One major disadvantage of ointments is that they leave a film over the patient's eye. Thus, the patient's vision can be impaired.

7-4. CHARACTERISTICS OF OPHTHALMIC PREPARATIONS

a. **Solutions**. Ophthalmic solutions must be sterile and particle-free. Moreover, ophthalmic solutions should be isotonic, if possible.

b. **Suspensions**. Ophthalmic suspensions must be sterile and free from large particles that might irritate the eye.

c. **Ointments**. Ophthalmic ointments must be sterile and free from large particles that irritate the eye.

7-5. PREPARATION OF OPHTHALMIC SOLUTIONS

Ophthalmic solutions are infrequently prepared in the pharmacy. When an ophthalmic solution is extemporaneously prepared, care must be taken to ensure that the preparation will benefit the patient. The following considerations are important when such a solution is being compounded.

a. **Prescribed Drug Present**. As with all pharmaceutical preparations, it is imperative that the ophthalmic solution contains the drug that is prescribed by the physician. Care must be taken to ensure that glassware used to compound the ophthalmic solution is not contaminated with other drugs. Why is this so important? As you probably know, certain drugs are used to treat glaucoma. If a drug that is contraindicated in glaucoma is administered to a patient who has glaucoma, damage to the patient's eyes could occur.

b. **Solution Sterile**. Certain bacteria can cause severe damage if they are instilled into the eye. Care must be taken to ensure that extemporaneously prepared ophthalmic solutions are sterile. Further, the sterile ophthalmic solution must be dispensed in a sterile container. Extemporaneously prepared ophthalmic solutions can be sterilized with a 0.22-micrometer membrane filter. Aseptic procedures must be used during this sterilization process.

c. **Solution Free from Visible Particles**. The ophthalmic solution must be free from visible particles. Remember that these visible particles could cause severe irritation if they were to be instilled into the eye. It is recommended that ophthalmic solutions be prepared in a laminar air-flow (LAF) hood, since the LAF hood provides an area that is practically free from visible particles.

d. **Solution Isotonic (if possible)**. In order to reduce tissue irritation, the ophthalmic solution should be made isotonic. In some cases, the concentration of the medication in the ophthalmic solution prevents the solution from being made isotonic (for example, the prepared solution is hypertonic).

7-6. DISPENSING OPHTHALMIC PREPARATIONS

a. **Solutions**. When dispensing an ophthalmic solution, the patient should be informed that the tip of the dropper should not be placed against an unclean surface.

b. **Ointments**. When dispensing an ophthalmic ointment, the patient should be informed that vision might be impaired for a short period after the ointment has been placed in the eye.

Continue with Exercises

EXERCISES, LESSON 7

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question or best completes the incomplete statement or by writing the answer in the space provided.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the group of definitions below, select the most correct definition of the term ophthalmic preparation.

   a. A sterile product intended to be applied to the eyelids or placed into the cornea.

   b. A sterile product intended to be applied to the eyelids or placed in the space between the eyelids and the eyeball.

   c. A sterile product intended to be applied to either the eyeball or the optic nerve.

   d. A sterile product designed to be injected in the muscle tissue surrounding the eye.

2. From the types of dosage forms listed below, select the type commonly used for ophthalmic preparations.

   a. Lotion.

   b. Elixir.

   c. Ointment.

   d. Emulsion.

3. From the list of characteristics below, select the characteristic required of ophthalmic suspensions.

    a. Particle-free.

    b. Isotonic.

    c. Sterile.

    d. Clear.

4. From the list of characteristics below, select the characteristic required of ophthalmic solutions.

    a. Isotonic.

    b. Neutral pH.

    c. Sterile.

    d. Colorless.

5. From the group of considerations below, select the consideration involved with the preparation of ophthalmic solutions.

    a. Ophthalmic solutions can be sterilized using paper filters.

    b. Ophthalmic solutions can be contaminated with other drugs without real concern for the patient’s welfare.

    c. The ophthalmic solution can contain some large particles as long as a “Shake Well Before Using” label is attached to the product.

    d. The ophthalmic solution should be made isotonic, if possible, to prevent irritation to the eye.

6. From the group of statements below, select the statement that contains the information the patient should be told when an ophthalmic ointment is being dispensed.

   a. Vision may be impaired for a short time after the ointment has been placed in the eye.

   b. The ointment should be stored in a freezer in order to maintain its sterility.

   c. Large particles in the ointment may be reduced in size by rapidly batting the eyes after the ointment has been applied.

   d. Large particles in the ointment may be removed by filtering the product through coarse grade gauze.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 7

1. b (para 7-1)
2. c (para 7-3b)
3. c (para 7-4b)
4. c (para 7-4a)
5. d (para 7-5d)
6. a (para 7-6b)

End of Lesson 7