Pharmacy Class of 2014

Study Buffalo Formulary

Pharmacy 331 Lab Final Study Guide

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Chapter 01

Percentages

The term %, when used without a w/v, v/v, or w/w designator typically means:

- % (w/v) for solutions or suspensions of solids in liquids
- % (v/v) for solutions of liquids in liquids
- % (w/w) for solid or semisolid mixtures

Different Molecular Forms (Salts, Hydrated Molecules)

Sometimes molecules don't come as a single molecule; they may be hydrated (Eg. $\cdot 2H_2O$) or come as a salt (Eg. HCl). If you have to use one of these you have to account for the increased weight due to the extra molecules, which can be done as a ratio of the molecular weights:

$$\frac{MW_{Drug+Salt/Water\ Molecules}}{MW_{Drug}} * m_{Drug}$$

The molecular weights of some common molecules/atoms

Molecules	Molecular Weight (g/mol)
H_2O	18.02
HCl	36.46
Na^+	22.99
SO_4^{2-}	96.06

Aliquots

The formulae in this formulary do not account for aliquots. Here are some hints when having to do an aliquot

- If possible, use a liquid in the prescription as a solvent and do a solid-liquid; this will reduce the changes you have to make to the prescription
    - Common solvents in many prescriptions are ethanol, water, propylene glycol and glycerine
    - A solution also has an even distribution of solute so you do not need to worry about proper mixing
- If the weight is close enough you can increase the total quantity of the prescription
    - This can account for both the issue of the MWQ and for any losses during compounding

Mixing Solids & Geometric Mixing

Comminution

- The reduction of particle size
- Three methods
    - Trituration: grinding of a powder in a mortar and pestle
    - Pulverization by Intervention: dissolution of a solid in a solvent, spreading the solution on an ointment slab and then recrystallization by evaporation of the solvent
    - Levigation: grinding of a powder in a mortar and pestle with a viscous insoluble liquid

Spatulate

- The mixing of powders with a spatula without reducing particle size

Geometric Mixing

- Used when mixing a small quantity with a larger quantity or when mixing solids into a liquid (to prevent clumping)

  Process

  1. Mix the small quantity with an equal quantity of the larger portion
  2. Mix the mixture with an equal quantity from the remaining larger portion
  3. Repeat step 2 until the two quantities are completely mixed

Accounting For Loss

None of the formulae in this formulary account for loss during compounding

Here are some common numbers to use when accounting for loss

Dosage Form	**Amount Extra**
Solutions	5%
Suspensions	5%
Emulsions	5%
Semisolids	2-3 grams or 5%
Suppositories	Make 2 extra for every 10
Powders	<5% (depending on skill)
Capsules (Hand Filled)	Make 1-2 extra for every 12
Capsule (Manual-Filling Machine)	<5% (depending on skill)

These are just suggestions and estimates; it can vary largely on comfort and skill

Bottle Calibration & Measuring Liquids

A bottle can be 'calibrated' by adding a known quantity of water (from a graduated cylinder) and marking the meniscus on the outside of the bottle

You can use this mark to then measure your compound into the bottle and be sure you have added enough and not have to worry about excess being left in the mortar/beaker/graduated cylinder

Expiry Date

Expiry dates depends on two factors: source of ingredients and water content

The following chart summarizes expiry dates for various dosage forms

	Water Present	**Water Absent**
Manufactured Drug Product or USP/NF Ingredients	14 days	6 months or 25% of closest expiry date (whichever is smaller)
Other Ingredients	14 days	30 days or duration of therapy (whichever is smaller)

Also remember that the day you compounded counts as the first day

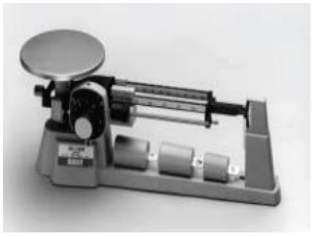
Example: If you compound a suspension with water (14 day expiry) on January 1, it expires on January 14

Chapter 02

Definitions

- Weighing
  - Ascertaining a definite weight of a material to be used in compounding a prescription or manufacturing a dosage form
  - Why is it important?
    - To have accurate dosage forms
    - Is a common source of error that could be difficult to detect in the final analytical results
- Balance
  - An instrument for determining the relative weights of substances
    - Weight is relative to another (typically a standard weight like grams)
  - Types of Balances
    - Equal-Arm Balances

    - Unequal-Arm Balances



    - Two Pan Torsion Type Balance

- Electronic Single Pan Balances
  - Higher sensitivity compared to most analogue balances
- Capacity
  - The maximum weight (including containers and tares) that can be placed on a balance pan
  - Maximum weight that can be weighed
- Sensitivity
  - The smallest weight that gives a perceptible change in the indicating element
  - The smallest weight that can be detected
- Accuracy
  - The closeness of the displayed weight (as measured by a balance) to the true weight, as known by the use of a calibration weight(s)
- Precision
  - The reproducibility of the weighing measurement as expressed by a standard deviation
- Prescription Balance
  - A scale or balance adapted to weighing medicinal and inactive ingredients in pharmaceutical compounding
  - Class A Prescription Balance
    - Must meet or exceed a sensitivity of 6mg with no load and a load of 10g

Process for Accurate Weighing

1. Planning
   - Choosing appropriate equipment
   - Containers
   - Preparing the material to be weighed
2. Checking the balance
   - Flat, level surface
   - Low vibrations and air currents
   - Clean and free of chemical contamination
   - Calibration
     - Tested at regular intervals for precision and accuracy with standard weights

3. Weighing the Material
    - Place a weighing paper on each balance pan
        - Never put weights, drugs or chemicals directly on a balance pan
        - Use glassine papers with glazed surfaced
        - Can fold to create a "boat"
        - Should not interfere with movement of pans
    - Bring balance pans into equilibrium to make sure both papers have the same weight (tarring the balance)
    - Add the weights with tweezers or forceps (never by hand)
    - Add the materials to be weighed with a spatula
    - Release the arresting mechanism
    - Weigh the material
    - Arrest the balance pans and remove the weights and weighted material
    - Clean the balance

Minimum Weighable Quantity (MWQ)

$$\% \, Error = \frac{Sensitivity}{Desired \, Amount}$$

$$MWQ = \frac{Sensitivity}{\% \, Error}$$

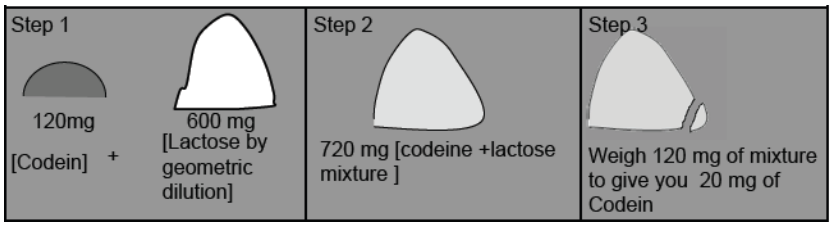
- USP standards state that error cannot be more than 5%
- Therefore there is a minimum quantity that can be weighed on a balance to achieve USP standards
- For a Class A Balance (sensitivity of 6mg), the MWQ is 120mg
- If you need a quantity less than the MWQ you must use aliquots

- Aliquots
    - Procedure
        1. Weigh or measure an amount of **drug** that is equal to or greater than the MWQ for that balance/device
        2. Weight or measure a compatible, inert diluent and mix with drug
            - Examples
                - Solids: Lactose
                - Liquids: Water or Alcohol
        3. Weigh or measure an aliquot (greater than or equal to the MWQ), which contains the desired amount of drug

- Solid-Solid Aliquots

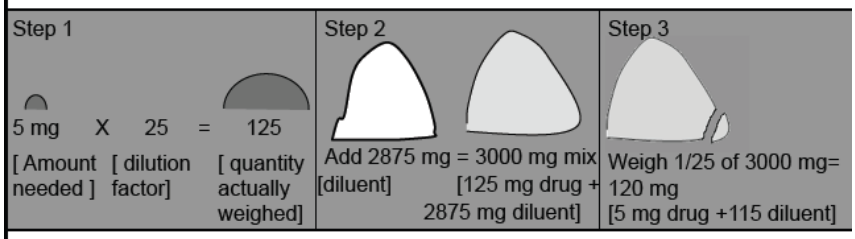
$$\frac{Amount\ of\ drug\ desired}{Amount\ of\ aliquot\ weighed} = \frac{Amount\ of\ dilution\ (drug)\ weighed}{Total\ amount\ of\ dilution\ (drug + diluent)}$$

  - Method 1 - Based on MWQ



  - Method 2 - Based on Dilution Factor

(1/ dilution factor) X = 120 mg (or desired weight of aliquot)
Where X is the total amount of dilution



On another look

$$\frac{5\ mg\ (drug\ needed\ for\ Rx)}{125\ mg\ (\ total\ drug\ weighed\ )} = \frac{120\ mg\ (drug\ diluent\ mix\ needed\ for\ Rx)}{3000\ mg\ (total\ amount\ of\ mix\ prepared)}$$

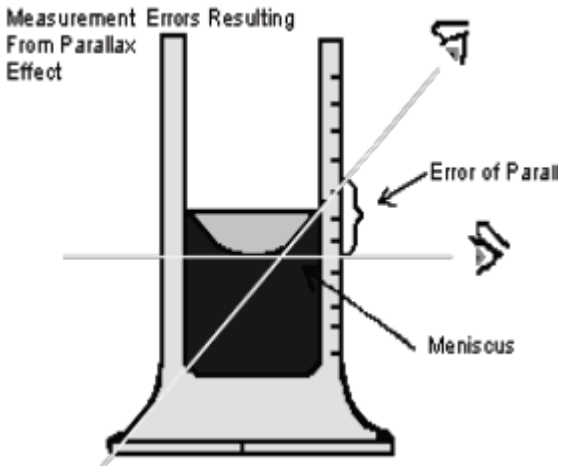
  - As a general rule, an amount of drug requiring a **dilution greater than 100:1 should not be done**
    - Homogenous mixing is difficult at this level
    - The amount of diluent needed becomes unreasonably large
    - **Best to use serial dilutions at this point**
- Solid-Liquid Aliquots
  - Used when the drug is to be incorporated into a liquid product
  - Advantages
    - Easier to make (dissolving is less time consuming that triturating)
    - Complete homogeneity
  - Basic Steps
    - Weigh the MWQ of the drug
    - Check solubility in the solvent
    - Dissolve in a convenient volume
    - Calculate the concentration

        - Calculate the volume of dilution needed for the desired amount of drug
        - Measure out the required volume
    - Liquid-Liquid Aliquots
        - Uses Minimum Measurable Quantity (MMQ)
            - There is nothing to weigh, so have to consider limitations of the measuring vessel
        - Basic Steps
            - Calculate the amount of the drug
            - Determine a convenient volume of final solution
            - Measure out the MMQ of the drug
            - Add water (qs) to reach the volume determined
            - Calculate the volume of solution needed
            - Measure out the required volume (equal to or greater than the MMQ)

Volumetric Measures

- Capacity
    - The designated volume, at the maximum graduation, which the vessel will contain or deliver at the indicated temperature
- Apparatus
    - Pipettes
        - Useful for smaller volumes (<2mL), which are usually below the MMQ for graduates
    - Burettes
    - Graduates
        - Cylindrical
            - Preferred over conical
        - Conical
    - Medicine droppers
        - Graduated
        - Non-graduated
- MMQ
    - General rule is to never measure less than 20% of the capacity of the apparatus

- Accurate reading



  - **Read at the meniscus line, not above it**

Chapter 03

Considerations When Preparing Solutions

- A true solution requires for the solute to be soluble in the solvent
    - Solubility in many common solvents can be found for most drugs in the Martindale or the Merck Index
    - Factors Affecting Solubility
        - Physio-chemical properties of the solute
        - Temperature
        - pH (degree of ionization)
        - Application of prodrugs
        - **These are the ones that can typically be changed while compounding:**
            - **Presence of co-solvents (eg. Alcohol)**
            - **Presence of solubilizing agents (eg. Surfactants)**
            - **Micronization of the solute particles**
- If the solute is not soluble, you can either add surfactants or co-solvents
    - Co-solvents are ingredients added to increase solubility
    - Co-solvents should be miscible in the solvent so that the mixture doesn't separate
- Trituration can be used to reduce solute particle size and increase the rate of dissolution
- When using alcohol, it is important to consider to total alcohol percentage (especially with children)

Formulae

2% Sodium Sulfathiazole in Water Solution

Sodium sulfathiazole	2%
Water	25mL

Procedure

1. Calculate the required weight of sodium sulfathiazole

   $$m_{sulfa} = 25mL * 0.02 = 0.5g$$

2. Weigh out the calculate amount
3. Transfer to a clean 100mL beaker
4. Add 25mL purified water
   - You don't need to "qs" because this is a solution; the change of volume due to sodium sulfathiazole in this case will be very minimal
5. Use a glass stir rod to stir the mixture until dissolved
6. Transfer to a prescription bottle

2.4 % Acetaminophen Cherry Syrup

Acetaminophen	2.4%
Alcohol	10%
Propylene Glycol	10%
Glycerine	30%
Sorbitol Solution	70%
Cherry Syrup	10%
Water	qs 80mL

Procedure

1. Calculate the required amounts

Ingredient	Prescription	Calculation	Final Measurement
Acetaminophen	2.4%	$80mL * 0.024$	1.92
Alcohol	10%	$80mL * 0.10$	8.0mL
Propylene Glycol	10%	$80mL * 0.10$	8.0mL
Glycerine	30%	$80mL * 0.30$	24mL
Sorbitol Solution	70%	$80mL * 0.70$	56mL
Cherry Syrup	10%	$80mL * 0.10$	8.0mL
Water	qs 80mL	qs 80mL	qs 80mL

2. Weigh out the required acetaminophen and transfer to a 150mL beaker
3. Measure out the alcohol, propylene glycol and glycerine and mix with acetaminophen one-by-one, stirring with a glass rod
4. Measure out the sorbitol solution and cherry syrup and mix with the acetaminophen solution
    - You want to add viscous solutions to less viscous ones to enable better mixing
5. Transfer the entire mixture to a 100mL graduated cylinder and qs to 80mL with purified water
6. Measure out the required amount for the prescription and transfer to a prescription bottle

Chapter 04

Considerations When Preparing Suspensions

- You want a small particle size to reduce the rate of sedimentation, but you need to keep the particles large enough to prevent aggregation
    - In general, it is better to triturate less and keep larger particles; it is easier to re-suspend a loose sediment than an aggregated one
- You can increase viscosity to reduce sedimentation, but you want it thin enough to pour
    - You can make thixotropic suspensions which thin with shaking (so it is pourable) and thicken when not moved (to slow down sedimentation on the shelf)

Formulae

2% Lidocaine in Calamine Lotion

Lidocaine	2%
Calamine Lotion	qs 180mL

Calamine Lotion USP

Calamine	80g
Zinc Oxide	80g
Glycerine	20mL
Bentonite Magma	250mL
Calcium Hydroxide Topical Solution	qs 1000mL

Procedure

- Calculate the amounts needed for 180mL of calamine lotion and for 2% lidocaine

Ingredient	USP	Calculation	Final Measurement
Calamine	80g	$\frac{80g}{1000mL} * 180mL$	14.4g
Zinc Oxide	80g	$\frac{80g}{1000mL} * 180mL$	14.4g
Glycerine	20mL	$\frac{20mL}{1000mL} * 180mL$	3.6mL
Bentonite Magma	250mL	$\frac{250mL}{1000mL} * 180mL$	45mL
Calcium Hydroxide Topical Solution	qs 1000mL	qs 180mL	qs 180mL
Ingredient	**Prescription**	**Calculation**	**Final Measurement**
Lidocaine	2%	$180mL * 0.02$	3.6g
Calamine Lotion	qs 180mL	$qs\ 180mL$	180mL

- Calculate how much Lidocaine HCl·H_2O is needed to give 2% lidocaine

$$\frac{MW_{Lidocaine\ HCl\cdot H2O}}{MW_{Lidocaine}} * m_{Lidocaine} = \frac{\frac{288.9g}{mol}}{\frac{234.3g}{mol}} * 3.6g = 4.44g$$

3. Measure the bentonite magma and dilute it with an equal volume of calcium hydroxide topical solution (to thin it out for easier mixing)
4. Weigh the lidocaine HCl·H_2O, calamine and zinc oxide and triturate together
5. Measure the glycerine and add it with 15mL of the bentonite magma:calcium hydroxide solution to the mortar and levigate until a smooth paste is formed
6. Gradually add the rest of the bentonite magma while continually mixing
7. Add about 25mL of the calcium hydroxide topical solution to the mortar to dilute the mixture into a pourable suspension
8. Pour the mixture into a graduated cylinder

9. qs with the calcium hydroxide topical solution by first rinsing it in the mortar and then pouring it into the graduated cylinder
10. Transfer to a prescription bottle , cap the bottle and shake well

5mg/mL Hydrochlorothiazide Suspension

Hydrochlorothiazide	5mg/mL
Citrucel (Methyl Cellulose in Water Solution)	1%
Sodium Benzoate	0.2%
Purified Water	qs 60mL

Procedure

1. Calculate the amounts needed for 60mL

Ingredient	Prescription	Calculation	Final Measurement
Hydrochlorothiazide	5mg/mL	$60mL * \frac{5mg}{mL}$	300mg
Methyl Cellulose	1%	$60mL * 0.01$	0.60g
Sodium Benzoate	0.2%	$60mL * 0.002$	0.12g
Purified Water	qs 60mL	$qs\ 60mL$	60mL

2. Levigate the methyl cellulose, sodium benzoate and hydrochlorothiazide with about 2mL of glycerine to wet the powders
3. Add 30mL of purified water **in portions** and mix with the powders
4. Transfer the suspension to a graduated cylinder
5. qs with purified water by first rinsing it in the mortar and then into the graduated cylinder
6. Transfer to a prescription bottle, cap the bottle and shake well

1% Clindamycin Lotion

Clindamycin	1%
Propylene Glycol	1.5mL
Isopropyl Alcohol (50%) & Purified Water	aa qs ad (sufficient quantity of each up to) 15mL

Procedure

1. Calculate the amounts required

Ingredient	**Prescription**	**Calculation**	**Final Measurement**
Clindamycin	1%	$15mL * 0.01$	0.15g
Propylene glycol	1%	$1.5mL * 0.001$	1.5mL
Isopropyl Alcohol 50% & Purified Water	aa qs ad 15mL	$aa\ qs\ ad\ 15mL$	aa qs ad 15mL
Ingredient	**For 15mL of IPA:Water**	**Calculation**	**Final Measurement**
IPA 70%		$\frac{15mL}{2} * 0.5 * \frac{1}{0.7}$	5.35mL
Purified Water	qs 30mL	qs 15mL	qs 15mL

2. Measure the IPA 70% and purified water and prepare the 50% IPA:Purified water solution
3. Weigh the clindamycin and place in a beaker and dissolve it with about 15mL of the 50% IPA:Purified Water solution
4. Allow the clindamycin to dissolve over 10-15 minutes with intermittent stirring over 10-15 minutes
5. Filter the solution through a filter paper
6. Add the propylene glycol to the solution and transfer to a graduated cylinder
7. qs to 15mL by rinsing the beaker with the IPA:Purified Water Solution and transferring to the graduated cylinder
8. Transfer to a prescription bottle, cap and shake well

Chapter 05

Considerations When Preparing Emulsions

- Consider what the purpose of the emulsion is
  - Oral emulsions are almost always O/W
  - The best emollients are W/O
  - You can create a depot effect with W/O/W emulsions
- Determining what type of emulsion it is
  - Phase Ratios
    - The external phase is typically present in greater concentrations
  - Order of Mixing
    - The phase that is being added in portions tends to be the internal phase
- HLB's and Surfactants
  - Emulsifier HLBs
    - HLB 3-6: Water in Oil (Ex. Span)
    - HLB 8-18: Oil in Water (Ex. Tween)
- When using a surfactant you need to know:
  - HLB of your surfactant
  - Required HLB of your ingredient (found experimentally)
  - Calculating required amounts of surfactants

    Calculate the fraction of each surfactant used (as a total of all surfactant; assume 5% of the total prescription volume/mass)

    $$Required\ HLB = (F_A * HLB_A) + (F_B * HLB_B) + \ \ldots$$
- Most emulsions require vigorous mixing, so choose the smallest mortar and the biggest pestle (that will fit) to increase your surface area between mortar and pestle

Methods of Preparation

Continental or Dry Gum Method (with Acacia)

Acacia is added to oils in different proportions depending on what type of oil it is

- Fixed Oils (cottonseed oil, mineral oil, etc.)
  - O:W:A = 4:2:1
- Essential Oils (Lavender oil, peppermint oil, etc.)
  - O:W:A = 3:2:1 or 2:2:1

Procedure

1. All acacia and oil is mixed together at once
2. Water is then added all at once
3. Hard and fast trituration
   - White appearance and crackling sound means it has been successful
   - Should occur within 2-3 minutes in most cases
4. After primary emulsion is formed you can add water miscible liquids
   - Water soluble solids can be dissolved before they are added to the primary emulsion
5. Insoluble ingredients can be added to the primary emulsion by trituration in portions

English or Wet Gum Method (with Acacia)

Acacia is added in the same ratios as used for the dry gum method

Procedure

1. Acacia is wetted with a wetting agent (ex. Glycerine)
2. All of the water is gradually added with mixing
3. Oil is added gradually with vigorous trituration
   - White appearance and crackling sound means it has been successful

Bottle Method

Procedure

1. Surfactant and oil are added together and mixed in bottle
2. Water is added to the bottle
3. Entire mixture is shaken vigorously

Beaker Method

Procedure

1. Dissolve the water soluble compounds in water
2. Dissolve the oil soluble compounds in oil
3. And the internal phase to the external phase and vigorously mix

Formulae

Topical Sunscreen Emulsion

Calamine	5%
Zinc Oxide	5%
Dioxybenzone	3%
Oxybenzone	3%
Almond Oil	25mL
Ethanol	6%
Acacia	qs
Water	qs 50mL

Procedure

1. Calculate the required amounts

Ingredient	**Prescription**	**Calculation**	**Final Measurement**
Calamine	5%	$50mL * 0.05$	2.5mL
Zinc Oxide	5%	$50mL * 0.05$	2.5mL
Dioxybenzone	3%	$50mL * 0.03$	1.5mL
Oxybenzone	3%	$50mL * 0.03$	1.5mL
Alcohol USP	6% Ethanol	$\frac{50mL * 0.06}{0.95}$	3.16mL
Almond Oil	25mL	$25mL$	25mL
Acacia	qs	$O:W:A = 4:2:1$ $25mL:12.5mL:6.25mL$	6.25mL
Water	qs 50mL	$50mL * 1.05$	52.5mL

2. Weigh the acacia and put it in a mortar
3. Measure the almond oil and triturate it with the acacia
4. Measure 12.5mL of water and add to the oil:acacia mixture and triturate rapidly to form a primary emulsion
5. Add some water to thin the emulsion
6. Weight the quantities of calamine, zinc oxide, dioxybenzone and oxybenzone and wet them with the emulsion in a mortar
7. Measure the alcohol USP and add it to the emulsion
8. Transfer to a graduated cylinder and qs with water in portions (making sure to rinse the mortar with the water before pouring into the cylinder)
9. Transfer into a prescription bottle, cap and shake well

Castor Oil Oral Emulsion

Castor Oil	5%
Tween 80	qs
Span 20	qs
Cherry Syrup	qs 50mL

Procedure

1. Calculated the required amounts, assume the fraction of surfactant is 5%

Ingredient	**Prescription**	**Calculation**	**Final Measurement**
Castor Oil	5%	$50mL * 0.05$	2.5mL
Tween 80	qs	$50mL * 0.05 * 0.84$	2.1g
Span 20	qs	$50mL * 0.05 * 0.16$	0.4g
Cherry Syrup	qs	$qs\ 50mL$	50.0mL

$$Required\ HLB\ of\ castor\ oil = (F_T * HLB_T) + (F_S * HLB_S)$$
$$14 = (F_T * 15) + ((1 - F_T) * 8.6)$$
$$5.4 = 6.4F_T \qquad F_T = 0.84 \qquad F_S = 0.16$$

2. Weigh the amounts of Span 20 and Tween 80 (in a calibrated bottle) with a dropper/syringe
3. Add the oil to the bottle and shake vigorously
4. Add the cherry syrup to the calibration mark and shake vigorously until the emulsion is formed

Chapter 06

Considerations When Preparing Semi-solids

- Definitions of Semi-Solids

Ointments	Semi-solids preparations incorporated into a **hydrocarbon base**
Creams	Semi-solid preparations incorporated into a **O/W emulsion**
Gels	Semi-solid preparations incorporated into either **suspensions of small inorganic particles or large organic molecules interpenetrated by a liquid**
Pastes	Semi-solids preparations of **large amounts of solid** incorporated into a base

- Types of Bases

Base Type	**Key Points**	**Examples**
Hydrocarbon	• No water absorption & anhydrous • Water insoluble/immiscible, not water washable • Can absorb most oils • Best emollient, occlusive	White Petrolatum White Ointment

Anhydrous Absorption	• Hydrocarbon base with O/W emulsifiers • Can absorb lots of water • Can absorb most oils • Water insoluble/immiscible, not water washable • Less occlusive than hydrocarbon bases • Can be used to incorporate aqueous liquids into hydrocarbon bases	Lanolin Aquaphor Aquabase Polysorb Hydrophilic petrolatum
W/O Emulsions	• Limited water absorption, but good oil absorption • Less occlusive and emollient activity • Water increases risk of microbial growth • Water insoluble/immiscible, not water washable	Hydrous Lanolin Cold Cream Eucerin Hydrocream Rose Water Ointment
Water Washable	• Can absorb small amounts water, water washable • Limited oil absorption • Water increases risk of microbial growth • Can "dry out" as water evaporates • Poor emollient and occlusive properties	Vanishing Cream Dermabase Velvachol Unibase Hydrophilic Ointment
Water-Soluble	• Limited water absorption, water washable • Limited oil absorption • Water increases risk of microbial growth • Compatibility problems, can be irritating	Polyethylene glycol ointment

- When incorporating solids, you want to reduce them down to the finest particle size possible so the semi-solid is not gritty or irritating
    - This can be done via trituration or levigation
    - Some chemicals like urea do not levigate or triturate into fine particles and so these should be dissolved and incorporated as a solution
- Levigating Agents
    - Choosing a Levigating Agent:
        - If the prescription has a liquid in it, use that first
        - Only use a small amount (<5% of the total mass) if adding one to the prescription
        - **Choose one that will be miscible with the base**
    - Don't Use A Levigating Agent When:
        - The powder is already fine
        - The quantity of solid is small (<5% of the total mass)
        - The semi-solid is soft afterwards
        - The final product is to be a stiff ointment or paste

Formulae

10% Urea, 5% Lactic Acid, 0.8% Neomycin Ointment

Urea	10%
Lactic Acid	5%
Neomycin Sulfate	0.8%
4% Methylparaben, 0.4% Propylparaben in Propylene Glycol	5%
White Petrolatum	qs 15g

Procedure

1. Calculate the required amounts

Ingredient	Prescription	Calculation	Final Measurement
Urea	10%	$15g * 0.1$	1.5g
Lactic Acid USP (90% w/w Lactic Acid)	5%	$\frac{15g * 0.05}{0.9}$	0.83g
Neomycin Sulfate	0.8%	$15g * 0.008$	0.12g
Methylparaben Solution	5%	$15g * 0.05$	0.75mL
White Petrolatum	qs 15g	$qs\ 15g$	15g

2. Calculate the amount of water needed to dissolve urea and the amount of span to emulsify it (2% of the formula) and the aliquot for neomycin (MWQ = 0.200g)

   Aliquot of neomycin

   $$\frac{0.12g}{2.25mL} = \frac{0.200g}{x} \qquad x = 3.75mL$$

   Can use the water of the neomycin to dissolve the urea

   Solubility of urea in water = 1g/1.5mL

   $$1.5g * \frac{1.5mL}{1g} = 2.25$$

   Span Needed

   $$0.02 * 15g = 0.3g$$

3. Prepare the solution of urea and neomycin measure out the required amount and keep it in a beaker on a tarred scale
4. Measure the lactic acid USP and the parabens stock solution and add to the other liquids

5. Weigh the span and the white petrolatum (can be calculated by subtracting the weight of span and the beaker's contents) and mix the two together on an ointment slab
6. Incorporate the liquids in portions, ensuring uniform mixing
7. Transfer to an ointment jar

Zinc Oxide Paste

Zinc Oxide & Starch	aa 12.5g
White Petrolatum	qs 50g

Procedure

1. Calculate the required amounts

Ingredient	Prescription	Calculation	Final Measurement
Zinc Oxide and Starch	aa 12.5g	$12.5g\ of\ each$	12.5g of each
White Petrolatum	qs 50g	$qs\ 50g$	qs 50g

2. Weigh the zinc oxide and starch and use that weight to determine how much white petrolatum to weigh
3. Spatulate the zinc oxide and starch together on an ointment slab
4. Incorporate both powders into a small amount of white petrolatum to form a smooth paste
5. Geometrically incorporate remaining white petrolatum, ensuring to remove any large clumps
6. Transfer to a ointment jar

Hydrocortisone Gel

Hydrocortisone	2%
Hydroxypropylcellulose	0.875g
Propylene Glycol	2.08g
Polysorbate 80	1.08g
Isopropyl Alcohol 70%	qs 50g

Procedure

1. Calculate the required amounts

Ingredient	Prescription	Calculation	Final Measurement
Hydrocortisone	2%	$50g * 0.02$	1.0g
Hydroxypropylcellulose	0.875g	$0.875g$	0.875g
Propylene Glycol	2.08g	$2.08g$	2.08g
Polysorbate 80	1.08g	$1.08g$	1.08g
Isopropyl Alcohol 70%	qs 50g	$qs\ 50g$	qs 50g (~45g)

2. 24 hours before hand, prepare the hydroxypropylcellulose gel; weigh the hydroxypropylcellulose and sprinkle it in portions over the IPA, allowing it to become thoroughly wetted without stirring and letting it sit overnight
3. Weigh the hydrocortisone and place it in the mortar
4. Levigate the hydrocortisone with the propylene glycol and polysorbate 80
5. Triturate the hydroxypropylcellulose gel into the mortar in portions until the gel is a uniform consistency
6. Transfer the gel to a ointment jar

Lidocaine HCl & Diphenhydramine HCl in PLO Gel

Lidocaine HCl	600mg
Diphenhydramine HCl	300mg
Poloaxmer lecithin organogel	qs 30g

Procedure

1. Calculate the required amounts (this gel can be made in a ratio of 1part polaxamer to 4 parts LIPS)

Ingredient	**Prescription**	**Calculation**	**Final Measurement**
Lidocaine HCl	600mg	$600mg$	600mg
Diphenhydramine HCl	300mg	$300mg$	300mg
Ingredient	**Preparing 30g**	**Calculation**	**Final Measurement**
Polaxamer	1 Part	$30g * 0.2$	6.0g
Lecithin Isopropyl Palmitate Solution	4 Parts	$30g * 0.8$	24g

2. Weigh the lidocaine HCl and Diphenhydramine HCl and place in a glass mortar
3. Measure out the polaxamer and the LIPS and stir together until a uniform gel is obtained
    - This may need to be heated over a water bath if room temperature is too low
4. Geometrically incorporate the gel into the powders until a smooth paste is obtained
5. Transfer the gel to an ointment jar

Chapter 07

Considerations When Preparing Suppositories

- Choose the right base for the location of insertion and the environment
  - Rectal Suppositories
    - Can be water-based (dissolving) or oleaginous (melting), but melting bases work quicker and are usually less irritating
    - Want to avoid bases that are humectants
  - Vaginal & Urethral Suppositories
    - Want to use water-based bases so that they don't melt and leak out
  - Melting suppositories may not be appropriate for warm climates
  - Water-based suppositories may not be appropriate for humid climates
  - Example Bases

Base	Base Type	Key Points
Cocoa Butter	Melting Base	• If overheated the base is liquid at room temperature • Melts at 37°C • Non-irritating
Synthetic Triglycerides	Melting Base	• Can't be overheated • Can have a range of melting points • Better contraction on cooling
Glycerinated Gelatine	Dissolving Base	• Humectant - important to add water before insertion • Glycerine A and Glycerine B are incompatible

PEG Mixtures	Dissolving Base	• Hygroscopic - important to add water before insertion • Many incompatibilities
Surfactant Bases	Dissolving Base	• Related to PEG and can be used as the vehicle or in combination with others • Have to consider effect of surfactant on drug release

- Non-ionized drugs are better absorbed for systemic action, but they are either trapped in oleaginous bases or inhibited by the slow dissolution of water-based bases and so ionized drugs provide better bio-availability
- If using metal moulds, contraction is important to ensure the base is removable

Methods of Preparation

Hand Rolling

1. Plastic-like mass is prepared by trituration of grated cocoa butter and active ingredients in a mortar
2. Mass is formed into a ball and rolled into a cylinder
3. Cylinder is cut into equal weights and rolled to produce a conical shape

Compression Moulding

1. Mixed mass of suppository base and drug is placed into a compression mould
2. Mixture is pressed into a suppository that is then removed

Fusion Moulding

1. Suppository base is melted and the drug is dispersed in the melted phase
    - Requires one to know mould weight and the density factor of the drug in the base or to double cast
        - Mould weight can be determined by casting blanks and weighing and averaging
        - Density factor can be determined from a reference or through double casting
    - Calculating base needed

$$m_{base\ displaced} = \frac{m_{drug}}{DF}$$

$$m_{base\ needed} = m_{blank} - m_{base\ displaced}$$

2. Mixture is removed from heat and poured into a suppository base
    - Metal suppository moulds **must** be lubricated
3. After cooling the suppositories are removed

Double Casting & Determining Density Factors

1. The total quantity of drug is measured with an amount of base that is inadequate to fill the number of cavities (based on the previously determined mould weight)
2. The mixture is poured into the mould, partially filling each cavity and the remaining is filled with blank base
    - The average weight of these suppositories can tell you how much a medicated suppository weighs
    - The density factor can then be calculated as follows:

$$Density\ Factor = \frac{m_{drug}}{m_{base\ displaced}}$$

$$m_{base\ displaced} = m_{blank} - (m_{medicated} - m_{drug})$$

3. The cooled suppositories are then removed, re-melted, mixed and re-cast to evenly distribute the ingredient

Formulae

Calculating the nominal weight and DF of iron in cocoa butter

Iron	200mg
Cocoa Butter	qs 8 suppositories

Procedure

1. Melt sufficient coca butter to fill 8 moulds (~16-18g), ensuring you do not overheat the cocoa butter
2. Fill the 8 moulds with cocoa butter, tap the mould to release any air bubbles and let cool
3. When cooled, remove any cocoa butter bulging from the top of the mould with a warm spatula and the remove the mould

4. Weigh the suppositories and calculate the average weight to determine the weight of a single suppository
5. Repeat steps 1-4, but do so with 1.6g (200mg * 8) of iron
6. Weigh the medicated suppositories and determine the density factor
7. Re-melt the medicated suppositories and evenly distribute the iron
8. Re-pour the suppositories, taking care not to overheat so the iron does not sediment too quickly
9. Allow the suppositories to cool and then remove from the moulds

Sulfathiazole Cocoa Butter Suppositories

Sulfathiazole	0.2g/suppository
Cocoa butter	qs for 6 suppositories

Procedure

1. Calculate the required amounts (assuming a mould weight of 2g and a DF of 1.6)

$$Sulfathiazole\ needed\ = 0.2g\ * 6 = 1.2g$$

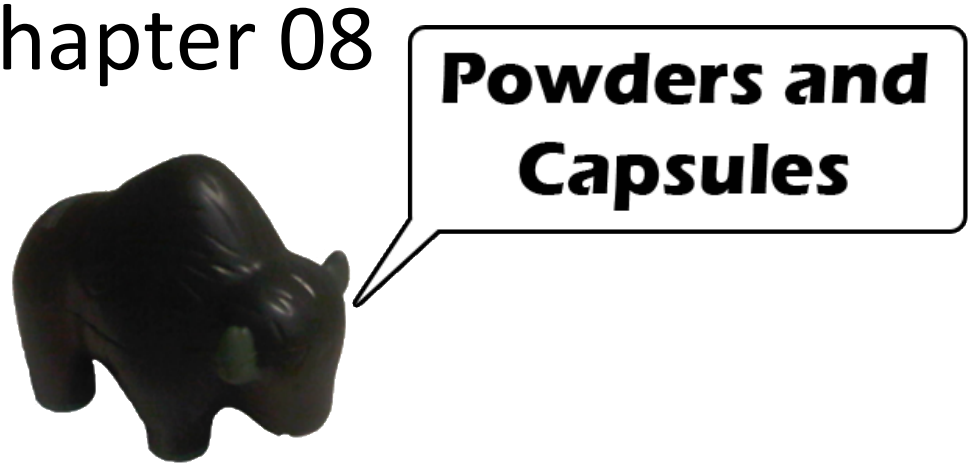
$$Base\ needed\ for\ blanks = \ 2g\ * 6 = 12g$$

$$Base\ displaced\ by\ sulfathiazole = \frac{1.6g}{1.6} = 1g$$

$$Base\ needed\ for\ medicated\ \ = 12g\ - 1g = 11g$$

2. Weigh the required amount of cocoa butter and melt it over a hot water bath
3. Once melted, incorporate the required sulfathiazole and stir until it is evenly distributed
4. Pour the mixture into suppository moulds and let cool
5. Remove any base that his bulging from the mould with a hot spatula or razor and then remove the suppositories from the mould

Chapter 08



Considerations When Preparing Powders & Capsules

- To ensure proper mixing of powders, they must be the same size
- When two powders are in different quantities, geometric addition should be used with trituration (or spatulation if no further particle reduction is required)
- When measuring volumes of powders you must consider both tapped densities and bulk density

$$Bulk\ Density = \frac{mass}{V_{untapped}} \qquad Tapped\ Density = \frac{mass}{V_{tapped}}$$

  - The procedure of tapping is by dropping the graduated cylinder (gently) ~20 times, recording the volume and then repeating the process until no further change occurs
  - Unless specified otherwise, the tapped density should be used for calculations for single dose packages or capsules
- The largest capsule size for human consumption is 00
- The amount of drug that fits in a capsule can be determined by filling blanks and then weighing the contents (following the same principle as double casting)

Methods of Preparation for Capsules

Punch Method

Typically requires 1-2 extra capsules for every ~12

Procedure

1. Prepare powders as required and then place on ointment slab in a compacted pile

2. Tare balance with weight paper and empty capsule shell
3. Take an empty capsule shell, remove the cap and "punch" powder into the capsule shell
4. Loosely cap the capsule and weigh it
5. Adjust weight as needed and when correct, close the capsule

Manual-Filling Machines

Does not require extra capsules to be prepared

Procedure

1. Prepare the powders are required
2. Assemble the filling machine as directed by the manufacturer
3. Load the capsules as directed and then remove the caps
4. Fill the bodies with powder, making sure to tap down the powder so that they are filled properly
5. Replace the caps and seal each capsule before removing from the machine

Formulae

Aluminum Hydroxide, Magnesium Trisilicate, Calcium Carbonate Powder

Aluminum Hydroxide	7.5g
Magnesium Trisilicate	7.5g
Peppermint oil	qs
Calcium carbonate	qs 30g

Procedure

1. Calculate the amounts required

Ingredient	Prescription	Calculation	Final Measurement
Aluminum Hydroxide	7.5g	$7.5g$	7.5g
Magnesium Trisilicate	7.5g	$7.5g$	7.5g
Peppermint oil	qs	qs	qs
Calcium carbonate	qs 30g	$qs\ 30g\ (\sim 15g)$	~15g

2. Measure out each ingredient and geometrically mix with a few drops of peppermint oil by trituration
3. If necessary weigh out single doses and seal in pharmaceutical paper or place in a ointment jar for bulk use

50mg Doxycycline Capsules

Doxycycline	50mg/capsule
Mannitol	qs for 30 capsules

Procedure

1. Calculate the required amounts
    a. Assuming each capsule holds 300mg of powder

Ingredient	Prescription	Calculation	Final Measurement
Doxycycline	50mg/capsule	$50mg * 30$	1.5g
Mannitol	qs for 30 capsules	$(30 * 300mg) - 1.5g$	7.5g

b. Assuming 30 capsules holds 15mL of powder (tapped)

Ingredient	Prescription	Calculation	Final Measurement
Doxycycline	50mg/capsule	$50mg * 30$	1.5g
Mannitol	qs for 30 capsules	$qs\ 15mL$	qs in graduated cylinder to 15mL

2. Measure out the required doxycycline and geometrically incorporate with the measured mannitol
3. Assemble capsule machine and capsules as directed
4. Fill capsules with mixed powder, making sure to tap volume down
5. Seal capsules as directed
6. Place capsules in vial or sealed bag

Acetaminophen, Diphenhydramine, Atropine Sulfate and Caffeine Capsules

Acetaminophen	325mg/capsule
Diphenhydramine HCl	25mg/capsule
Atropine Sulfate	0.12mg/capsule
Caffeine	30mg/capsule
	qs for 6 capsules

Procedure

1. Calculate the required amounts

Ingredient	Prescription	Calculation	Final Measurement
Acetaminophen	325mg/capsule	$325mg * 6$	1950mg
Diphenhydramine HCl	25mg/capsule	$25mg * 6$	150mg
Atropine Sulphate	0.12mg/capsule	0.12mg * 6	0.72mg
Caffeine	30mg/capsule	$30mg * 6$	180mg

2. Measure out the required ingredients

3. Add atropine to the mortar and geometrically mix with caffeine by trituration
4. Geometrically mix diphenhydramine HCl to the mixture by trituration
5. Geometrically mix acetaminophen to the mixture by trituration
6. Transfer to an ointment slab and compact mixture
7. Tare a balance with a weigh paper and empty capsule
8. Punch fill each capsule until the desired weight is reached
9. Seal each correctly filled capsule and place in a vial or bag

Appendix 1

Minimum Weighable Quantity (MWQ)

$$\%\ Error = \frac{Sensitivity}{Desired\ Amount}$$

$$MWQ = \frac{Sensitivity}{\%\ Error}$$

Aliquots (Solid-Solid)

$$\frac{Amount\ of\ drug\ desired}{Amount\ of\ aliquot\ weighed} = \frac{Amount\ of\ dilution\ (drug)\ weighed}{Total\ amount\ of\ dilution\ (drug + diluent)}$$

Henderson-Hasselbalch

$$\mathrm{p}H = pKa + \log(\frac{[A^-]}{[HA]})$$

Solubility

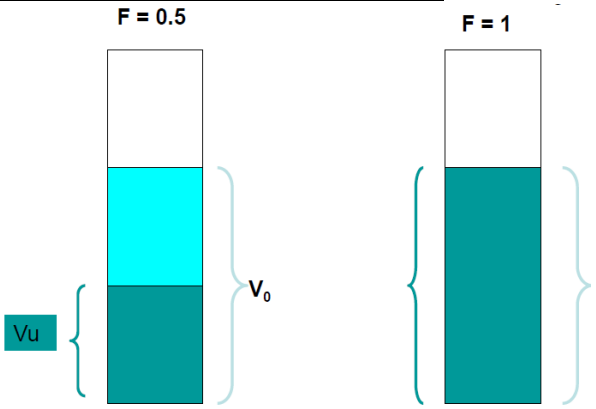
Acids

$$pH\ - pKa = \log\left(\frac{S_t - [HA]}{[HA]}\right)$$

Bases

$$pKa\ - pH = \log\left(\frac{S_t - [B]}{[B]}\right)$$

Sedimentation Volume



$$F = \frac{Vu}{Vo}$$

V_U = Volume of sediment

V_0 = Original volume

Required HLB

$$Required\ HLB = (F_A * HLB_A) + (F_B * HLB_B) + \ \ldots$$

F = fraction of surfactant

Density Factors

$$Density\ Factor = \frac{m_{drug}}{m_{base\ displaced}}$$

$$m_{base\ displaced} = m_{blank} - (m_{medicated} - m_{drug})$$

Bulk and Tapped Densities

$$Bulk\ Density = \frac{mass}{V_{untapped}} \qquad Tapped\ Density = \frac{mass}{V_{tapped}}$$