B. Pharmacy 1st Semester - Pharmaceutics I (UNIT – 2) 📚

Pharmaceutical Calculations 🧮

📏 Weights and Measures

Before dispensing medications, pharmacists must possess comprehensive knowledge of various calculation types and measurement systems. Understanding weights and measures forms the foundation of accurate pharmaceutical calculations.

Weight is defined as the measure of gravitational force acting on a body, directly proportional to its mass. **Measure** refers to the measurement of volume of any substance.

🏛️ Imperial System

The Imperial system represents an ancient measurement framework based on arbitrary and unrelated units including grains, drachms, ounces, and gallons. This system encompasses two distinct measurement categories for weight determination:

⚖️ Avoirdupois System

In the Avoirdupois system, the "pound" serves as the fundamental standard unit for weight measurement. All mass measures derive from the Imperial standard pound (Lb).

Key Conversions:

- 1 pound (Lb) = 16 ounces (oz)
- 1 pound = 7000 grains
- 1 ounce (oz) = 437.5 grains
- 437.5 grains = 1 oz = 28.35 gm
- 7000 grains = 1 Lb = 16 oz = 454 gm
- 1 kg = 2.2 Lb
- 1 grain = 64.8 mg

This system primarily utilizes weight measurements for pharmaceutical compounding purposes.

💊 Apothecaries System

The Apothecaries system incorporates both volume and weight measurements, specifically designed for compounding and concentration preparation for dilution. Weight measurements utilize grains, while volume measurements employ minims.

Volume Measurements:

- 1 teaspoonful (tsp) = 5 milliliters (ml) = 1 dram = 5 cubic centimeters (cc)
- 1 tablespoonful (tbsp) = 15 milliliters (ml)
- 29.57 milliliters (ml) = 1 fluid ounce (fl oz)
- 473 milliliters (ml) = 1 pint (pt) = 16 fluid ounces (fl oz)
- 946 milliliters = 1 quart = 2 pints
- 3784 milliliters = 1 gallon = 8 pints = 128 fl oz

Weight Measurements:

- 1 grain = 64.8 mg
- 1 ounce = 31.1 gm = 480 grains

📐 Metric System

The metric system, implemented in India's pharmacy profession from April 1st, 1964, serves as the standard measurement system used in the Indian Pharmacopoeia. This system operates by combining various prefixes (kilo-, hecto-, deka-, deci-, centi-, milli-) with base measurement units (meter, liter, gram).

Weight Measurements in Metric System: The kilogram represents the standard unit for weight measurement, with all other measures derived from it:

- 1 kilogram (kg) = 1000 grams
- 1 gram = 1000 mg
- 1 milligram (mg) = 0.001 gram
- 1 microgram (mcg) = 0.000,001 gram
- 1 hectogram (hg) = 100 grams
- 1 decagram (dag) = 10 grams

Latin Term	English Name	Equal To
Granum	Grains	1 grain
Scrupulus	Scruple	20 grains
Drachma	Drachm	60 grains
Uncia oz.	Ounce (Avoir)	437.5 grains
Uncia (Troy)	Ounce (Apothe)	480 grains
Libra	Pound (Avoir)	7000 grains
Libra	Pound (Apothe)	5760 grains

🔄 Alligation Method

The alligation method serves as a calculation technique employed when mixing two similar preparations of different strengths to produce a preparation of intermediate strength. This method provides an effective means of checking calculations and ensuring accuracy.

Application Process: When pharmaceutical preparations require mixing to achieve specific concentrations, the alligation method determines the precise proportions of each component needed. The method involves identifying the higher concentration, lower concentration, and desired final concentration, then calculating the required ratios through cross-multiplication techniques.

🧪 Calculations Involving Percentage Solutions

Pharmaceutical practice commonly utilizes four distinct types of percentage solutions:

1. **% w/v (Percentage weight in volume)** - Grams of solute per 100 milliliters of solution
2. **% v/v (Percentage volume in volume)** - Milliliters of solute per 100 milliliters of solution
3. **% w/w (Percentage weight in weight)** - Grams of solute per 100 grams of solution
4. **% w/W (Percentage weight in weight)** - Alternative notation for weight in weight

Common Formulas for Percentage Calculations:

For 1% w/v solution preparation in the imperial system, specific ratios apply when small volumes and weak solution strengths are required:

Solid	Solvent	To Produce
1 gm	110 ml	1% w/v solution
4.375 gm	1 fluid ounce	1% w/v solution
3.5 gm	8 fluid ounces	1% w/v solution

For standard 1% w/v solution preparation:

Solid	Solvent	To Produce
1 gm	100 ml	1% w/v solution

🍷 Proof Spirit

Proof spirit represents a specific mixture of alcohol and water that, at 51°F, weighs 12/13th of an equal volume of water. Alcohol strength calculations utilize proof degrees as the measurement standard.

Indian Standards:

- 100% proof spirit = 57% v/v ethyl alcohol
- Values exceeding 57% = over proof spirit
- Values below 57% = under proof spirit

Conversion Methods:

From Percentage Strength to Proof Strength: Multiply the percentage strength by 1.735 and subtract 100. Positive results indicate over proof, while negative results indicate under proof.

From Proof Strength to Percentage Strength: Divide the proof strength by 1.735, then add 100 for over proof or subtract 100 for under proof conditions.

🧬 Isotonic Solutions Based on Freezing Point and Molecular Weight

Definition and Importance: Isotonic solutions possess identical osmotic pressure and salt concentration. Physiologically, these solutions maintain the same osmotic pressure as body fluids when separated by biological membranes. Blood and lachrymal fluid normally exhibit osmotic pressure corresponding to 0.9% w/v sodium chloride solution.

Types of Tonicity:

Hypotonic	Isotonic	Hypertonic
NaCl 0.2%	NaCl 0.9%	NaCl 2%
Solute outside > inside	Solute outside = inside	Solute outside < inside
Cell swelling	Equilibrium	Cell shrinkage

Freezing Point Methods: Colligative properties, including osmotic pressure and freezing point depression, remain independent of dissolved substance nature. Blood plasma and tears freeze at -0.52°C, indicating that dissolved substances depress the freezing point by 0.52°C below pure water. Any solution freezing at -0.52°C possesses identical osmotic pressure to blood plasma and tears.

Calculation Formula: Percentage w/v of adjusting substance needed = $(0.52 - a) / b \times 100$

Where:

- a = Freezing point of unadjusted solution
- b = Freezing point of 1% w/v solution of adjusting substance

Molecular Concentration Method: Molecular concentration refers to the number of units (molecules, ions, or both) present in solution. A solution containing one gram molecule of non-ionizing solute in 22.4 liters at NTP possesses one atmosphere osmotic pressure. Blood plasma and lachrymal secretion osmotic pressure approximates 6.7 atmospheres, making a 0.3 M solution of any non-ionizing substance iso-osmotic with blood plasma and tears.

Powders

📋 Definition and Classification

A powder represents a homogeneous mixture of finely divided particles or materials in dry form, constituting a solid dosage form for internal and external medicinal use. Powders exist in both crystalline and amorphous forms.

✅ Advantages of Powders

Pharmaceutical powders provide numerous benefits including flexibility in drug selection, enhanced stability compared to other dosage forms, rapid therapeutic effects, ease of administration across all patient categories, economic advantages due to simplified manufacturing techniques, and reduced incompatibility risks.

❌ Disadvantages of Powders

Limitations include inability to dispense bitter, nauseous, or unpleasant-tasting drugs in powder form, unsuitability for deliquescent and hygroscopic drugs, inappropriate for drugs affected by atmospheric conditions, and challenges in maintaining uniform dosing.

🏷️ Classification of Powders

📦 Divided Powders

Unit dose powders requiring proper packaging, subdivided into:

Simple Powders: Contain single ingredients in crystalline or amorphous form, with finely divided powder weighed and wrapped as individual doses.

Compound Powders: Contain two or more substances mixed together and divided into individual doses.

📊 Bulk Powders for Internal Use

Dispensed when dosage accuracy remains less critical, containing several doses supplied in wide-mouthed containers permitting easy spoonful removal. Non-potent substances like antacids and laxatives typically utilize this format.

🧴 Bulk Powders for External Use

Non-potent substances supplied in specialized containers (cardboard, glass, or plastic) designed for specific application methods. Dusting powders utilize perforated or sifter-top containers with external application labels.

Common External Application Types:

- **Dusting Powders:** Applied to intact skin in fine subdivision to prevent irritation
- **Insufflations:** Introduced into body cavities using insufflator apparatus
- **Snuffs:** Inhaled into nostrils for antiseptic, bronchodilator, and decongestant effects
- **Dentifrices:** Tooth cleaning powders containing soap/detergent, mild abrasives, and anticariogenic agents

🥄 Powders Enclosed in Cachets (Wafer Capsules)

Cachets represent solid unit dosage forms molded from rice paper, created by pouring rice flour and water mixture between hot, polished revolving cylinders. Available in various sizes accommodating 0.2 to 1.5 grams of powder.

Advantages and Disadvantages:

Advantages	Disadvantages
Easy preparation without complex machinery	Require softening before swallowing
Immediate stomach disintegration	Easily damaged
Simple dispensing	Cannot protect from light and moisture
Large quantity accommodation (up to 1.5g)	Brittle shell construction
	Unsuitable for large-scale manufacturing

Types:

- **Wet Seal Cachets:** Two convex halves with flat edges, sealed using water
- **Dry Seal Cachets:** Upper and lower halves with different diameters, machine-sealed

💊 Compressed Powders (Tablet Triturates)

Small cylindrical molded or compressed tablets containing potent drugs mixed with lactose and binders like powdered acacia. The mixture undergoes moistening to create moldable, compatible mass, forced into mold board holes, ejected using peg boards, dried, and dispensed.

🛸 Dispensing of Powders

Special considerations apply when dispensing powders containing volatile substances, hygroscopic and deliquescent compounds, eutectic mixtures, efflorescent powders, liquids, explosive substances, and potent drugs.

Volatile Substances: Vegetable powders containing volatile oils require light mortar powdering to prevent oil loss. Substances like menthol, camphor, and essential oils necessitate double wrapping with inner wax paper and outer thick paper wrappers.

Hygroscopic and Deliquescent Powders: Hygroscopic powders absorb atmospheric moisture without dissolving, while deliquescent powders absorb moisture and dissolve. These substances require granular form supply, minimal powdering, double wrapping, and additional aluminum foil or plastic covering in humid conditions.

Efflorescent Powders: Crystalline substances liberating water of crystallization during atmospheric exposure or trituration. Solutions include using corresponding anhydrous salts or mixing with inert substances before incorporation.

Eutectic Mixtures: Substances that liquefy upon mixing due to compound formation with lower melting points than individual components. Dispensing methods include separate powder sets or mixing with inert absorbents like magnesium carbonate, light magnesium oxide, kaolin, starch, lactose, or calcium phosphate.

🔄 Mixing of Powders

Methods include:

Spatulation: Powder mixing using spatula movement on paper or porcelain tiles, suitable for small quantities and eutectic-forming substances.

Trituration: Grinding powder in mortar and pestle for particle size reduction and mixing, with porcelain mortars preferred for rough surfaces and glass mortars for smooth surfaces.

Geometric Dilution: Used for potent substance mixing with large diluent amounts, involving stepwise equal volume additions with trituration.

Sifting: Powder mixing through sifters, producing light fluffy products unsuitable for potent drug incorporation.

Tumbling: Large container powder mixing using electric motor rotation, widely employed in industrial large-volume applications.

💧 Liquid Dosage Forms

📖 Definition and Classification

Liquid dosage forms, designed for internal, external, or parenteral use, classify into monophasic and biphasic systems. Monophasic forms consist of true solutions, colloidal solutions, or solubilized systems with single phases and aqueous or non-aqueous solvent bases. Biphasic forms include emulsions and suspensions with two immiscible phases: continuous and dispersed.

✅ Advantages of Liquid Dosage Forms

Liquid formulations provide rapid onset of action compared to tablets and capsules, enable administration of medications requiring liquid form (such as castor oil), allow suspended drug delivery for maximum surface area exposure, prevent pain and irritation from dry drug forms, and offer psychological patient satisfaction.

❌ Disadvantages of Liquid Dosage Forms

Limitations include required dose measurement, stability and preservation challenges, proper storage requirements, container breakage risks during transport, and higher costs compared to solid dosage forms.

🧪 Excipients Used in Liquid Dosage Form Formulation

🍯 Sweetening Agents

Classified as nutritive (caloric) or non-nutritive (non-caloric), sweeteners enhance palatability and patient compliance.

Sucrose: White crystalline powder, water and alcohol soluble, inhibiting microorganism growth above 65% w/V concentrations. Official simple syrup contains 85% w/V sucrose in water.

Saccharin: Non-nutritive synthetic sweetener with approximately 500 times sucrose sweetening power.

Sucralose: Heat-stable sweetener approximately 600 times sweeter than sucrose.

Acesulphame-K: Heat-stable sweetener approximately 200 times sweeter than sucrose.

🌊 Viscosity Controlling Agents

Achieved through increased sugar concentration or incorporating agents like polyvinylpyrrolidone and cellulose derivatives. Carboxymethylcellulose functions in high alcohol concentrations (up to 50%) without precipitation, while methylcellulose polymers resist metal ion precipitation but may precipitate when electrolyte concentrations exceed limits.

⚖️ Buffers

Prevent pH changes during storage caused by product degradation, container component interactions, or gas/vapor dissolution. Suitable buffer systems require adequate capacity for pH maintenance while considering ionic strength contributions affecting stability. Common buffers include phosphates, acetates, citrates, and glutamates.

🛡️ Antioxidants

Prevent oxidative degradation of dissolved drugs by possessing lower oxidation potentials than protected substances. Examples include citric acid, ascorbic acid, EDTA, BHT, and BHA.

🍓 Flavors

Address four basic taste sensations (salty, bitter, sweet, sour) through careful selection and evaluation. Combination flavoring agents effectively mask undesirable tastes, with menthol, chloroform, and various salts serving as flavor adjuncts and desensitizing agents.

Taste Sensation	Recommended Flavors
Salt	Maple, apricot, peach, vanilla, wintergreen mint
Bitter	Wild cherry, walnut, chocolate, mint combinations, passion fruit, mint spice, anise
Sweet	Fruit and berry, vanilla
Sour	Citrus flavors, licorice, root beer, raspberry

🦠 Preservatives

Ideal preservatives demonstrate broad-spectrum antimicrobial effectiveness, physical/chemical/microbiological stability throughout product lifetime, non-toxicity, adequate solubility, formulation compatibility, and acceptable taste/odor characteristics.

Classification includes:

- **Acidic:** Phenol, chlorocresol, parahydroxybenzoic acid alkyl esters, benzoic acid salts, boric acid salts, sorbic acid salts
- **Neutral:** Chlorobutanol, benzyl alcohol, phenylethyl alcohol
- **Mercurial:** Thiomersal, phenylmercuric compounds, nitromersol
- **Quaternary Ammonium:** Benzalkonium chloride, cetylpyridinium chloride

💊 Solubility Enhancement Techniques

🔬 Pharmaceutical Approaches

pH Adjustments: Weak acid and base solubility significantly responds to pH modifications. Weak base solubility increases through pH reduction, while weak acid solubility improves through pH elevation. pH adjustment achieves through salt formation or buffer addition.

Cosolvency: Increases poorly soluble drug solubility by adding miscible solvents with high drug solubility. Cosolvents like ethanol, glycerol, propylene glycol, or sorbitol decrease interfacial tension, alter dielectric constants, and enhance weak electrolyte and non-polar molecule water solubility.

Complexation: Enhances poorly soluble drug solubility through soluble material interaction forming reversible intermolecular complexes, ensuring free drug release during biological fluid contact.

Surface Active Agents: Reduce interfacial tension between solute and solvent, forming thermodynamically stable homogeneous systems through micelle formation. At Critical Micelle Concentration (CMC), surfactant molecules aggregate into 100-150 molecule micelles. Solubilizing surfactants typically possess HLB values exceeding 13.

Hydrotropism: Describes aqueous solubility increases using large additive concentrations (20-50%), enhancing caffeine and theophylline solubility through sodium benzoate and sodium salicylate addition respectively.

Micronization: Inversely relates surface area and particle size, with smaller particles providing larger surface areas and greater solubility through micronization-achieved particle size reduction.

Solid Solutions: Prepared through physical mixture melting, also termed molecular dispersions or mixed crystals, demonstrating enhanced dissolution rates compared to pure substances.

Chemical Modification: Improves substance solubility through chemical modification, particularly increasing aqueous solubility by incorporating additional polar groups within molecular structures.

🛸 Stability Considerations

Physical, chemical, and microbiological stability require comprehensive consideration throughout liquid dosage form development, ensuring product integrity, efficacy, and safety throughout intended shelf life periods.