A TEXT BOOK

PHARMACY INDIA PUBLICATION

GENERAL PHARMACY

BP102T

As per NEP 2020

Bachelor of Pharmacy

1st Semester

Author

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FULLY COLOURED BOOK

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PREFACE

Pharmacy is a dynamic healthcare profession concerned with the discovery, preparation, quality, distribution and safe use of medicines. This book, General Pharmacy for B. Pharm First Semester, has been prepared according to the Pharmacy Council of India syllabus framed under NEP 2020 to provide students with a strong foundation in pharmaceutical sciences.

The book covers the history and scope of the pharmacy profession, pharmacy education and industry in India, professional organisations, pharmacopoeias, prescriptions and commonly used Latin terminology. It also explains the roles and responsibilities of pharmacists in community, hospital, clinical and industrial pharmacy.

Important topics such as pharmaceutical calculations, posology, routes of drug administration, dosage forms, active pharmaceutical ingredients and excipients are presented in a simple and systematic manner. Solid dosage forms, including powders, tablets and capsules, are discussed along with their classification, advantages, formulation ingredients and methods of preparation.

The book also includes monophasic and biphasic liquid preparations, suspensions, emulsions and semisolid dosage forms such as ointments, creams, pastes, gels, suppositories and pessaries. Special emphasis has been given to formulation principles, excipients, preparation methods and practical pharmaceutical applications.

A major feature of this book is the use of colourful visual graphics, labelled images, diagrams, flowcharts, tables and comparison charts to simplify difficult concepts and make learning more engaging. It is hoped that this student-friendly book will support conceptual understanding, examination preparation and the development of competent, ethical and responsible pharmacy professionals.

Authors

GENERAL PHARMACY SYLLABUS

1. Introduction to the Profession of Pharmacy — HOURS: 09

- **History of the Profession of Pharmacy in India:** In relation to pharmacy education, pharmaceutical industries and organizations – evolution, development and milestones.
- **Scope of the Pharmacy Profession:** Role and responsibilities of pharmacists in retail/community pharmacy, hospital and clinical pharmacy, and industrial pharmacy including research and development.
- **Pharmacopoeias:** Introduction to IP, BP, USP, BPC, International Pharmacopoeia, other pharmacopoeias and the National Formulary of India; structure and content of the Indian Pharmacopoeia; study of one model IP monograph.
- **Introduction to Prescription:** Structure and format/parts of prescription, handling of prescriptions, Latin terminology related to prescriptions.

2. Introduction to Pharmaceutical Calculations and Dosage Forms — HOURS: 09

- **Metric system of weights and measures;** calculations based on alligation, proof spirit, isotonic solutions, dilute solutions (percentage and ratio) and geometric dilution; scientific notation of units and measures.
- **Posology:** Definition and dose calculation based on age, body weight and body surface area. Introduction to Dosage Forms: Routes of administration and classification of dosage forms.
- **Introduction to Active Pharmaceutical Ingredients and Excipients:** Definition, ideal characteristics and importance.

3. Solid Dosage Forms — HOURS: 09

- **Powders:** Classification, advantages and disadvantages; dusting powders, effervescent powders, efflorescent powders, hygroscopic powders and eutectic mixtures; introduction to excipients and methods of preparation.
- **Tablets:** Definition, types of tablets including moulded tablets and pills with examples; advantages and disadvantages; introduction to excipients and methods of preparation.
- **Capsules:** Definition, types of capsules, advantages and disadvantages, capsule sizes; introduction to excipients and methods of preparation.

4. Monophasic and Biphasic Liquids — HOURS: 09

- **For internal use:** aromatic waters, syrups, elixirs and linctus (definition and preparation).
- **For external use and body cavities:** liniments, lotions, throat paints, applications, gargles, mouthwashes, enemas, eye drops, ear drops, nasal drops and tinctures with examples.
- **Study of official preparations:** Introduction to excipients and methods of preparation. Suspensions: Definition and types (flocculated and deflocculated), advantages and disadvantages, formulation excipients and general methods of preparation.
- **Emulsions:** Definition and types, emulsifying agents, tests for identification of types of emulsions, formulation excipients and general methods of preparation.

5. Semisolid Dosage Forms and Suppositories/ Pessaries — HOURS: 09

- **Semisolid Dosage Forms:** Definitions, classification, advantages and disadvantages, ointment bases and other excipients used in semisolid dosage forms; general methods of preparation of ointments, pastes, creams and gels.
- **Suppositories/ Pessaries:** Definition, types of suppositories, advantages and disadvantages, formulation excipients used in suppositories, properties of ideal suppository bases, types of suppository bases, displacement value and general method of preparation. topics covered in this book

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1 INTRODUCTION TO THE PROFESSION OF PHARMACY

- **History of the Profession of Pharmacy in India:** In relation to pharmacy education, pharmaceutical industries and organizations – evolution, development and milestones.
- **Scope of the Pharmacy Profession:** Role and responsibilities of pharmacists in retail/ community pharmacy, hospital and clinical pharmacy, and industrial pharmacy including research and development.
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1.1 INTRODUCTION

The discipline of pharmacy is an applied clinical and scientific profession dedicated to the discovery, development, production, standardization, and safe dispensing of medications. Over thousands of years, the profession has undergone a remarkable evolution, transitioning from ancient healers mixing crude herbal decoctions to modern pharmaceutical scientists developing highly targeted genomic therapies.

1.1.1 The Global Ancient History of Pharmacopeial Practices

In ancient times, the disciplines of medicine and pharmacy were virtually indistinguishable. The earliest pharmaceutical practices were deeply intertwined with botany, empirical observation, and spiritual beliefs. During the ancient and medieval eras, pharmaceutical practice was dominated by topical applications and liquid mixtures, relying heavily on herbal decoctions and poultices as the primary methods of drug delivery.

The evolution of the "pharmacopoeia" a term derived from the Greek words pharmakon (drug) and poiein (to make) began with the meticulous documentation of these ancient remedies across various global civilizations.

Mesopotamia: The Dawn of Documented Apothecary (2600 BCE)

- **Clay Cuneiform Tablets:** Medical practitioners recorded their symptoms, prescriptions, and compounding directions on clay tablets using cuneiform script.
- **The Healers:** Medical practice was divided between the ashipu (who relied on magical and spiritual healing) and the asu (the empirical healer). The asu functioned as early pharmacists, compounding botanical, mineral, and animal materials into plasters, ointments, and medicinal beers (Figure 1.1).

Figure 1.1: The Dawn Of Writing: An Ancient Mesopotamian Cuneiform Tablet

Ancient Egypt: The Formulation of Prescriptions (1550 BCE)

- **The Ebers Papyrus (1550 BCE):** This ancient Egyptian scroll is a critical milestone in global pharmacy, containing over 876 distinct prescriptions (Figure 1.2).
- **Early Dosage Forms:** It details the preparation of early dosage forms, including decoctions and pills, serving as one of the earliest documented pharmaceutical formulations in human history.

Figure 1.2: The Ebers Papyrus an Ancient Egyptian Medical Manuscript

to develop, validate, and standardize the rigorous analytical testing protocols that are ultimately published in the Indian Pharmacopoeia.

1.2.4 The Rise of the Indian Pharmaceutical Industry

With a solid educational pipeline overseen by the PCI and a strict regulatory framework managed by the CDSCO, the stage was set for the Indian pharmaceutical industry to evolve from small-scale domestic operations into a dominant global force.

Post-Independence Self-Reliance and the Generic Revolution

Post-1947, the new Indian government aggressively promoted domestic self-sufficiency. The state heavily invested in public undertakings, notably establishing Hindustan Antibiotics Ltd. in 1954 as Asia's first publicly owned penicillin factory, followed by entities like IDPL in 1961.

However, the defining turning point for the modern industry occurred with the Indian Patents Act of 1970 (heavily supported by the 1975 Hathi Committee). This landmark legislation boldly recognized process patents but deliberately refused to recognize product patents for medicines. This legal maneuver empowered Indian scientists and chemical engineers to legally reverse-engineer expensive foreign molecules and develop highly cost-effective manufacturing processes. This catalyzed a massive generic revolution. During the 1970s and 80s, ambitious private companies like Cipla, Ranbaxy, Dr. Reddy's, Sun Pharma, and Lupin aggressively developed and exported generic versions of vital therapeutics, fundamentally transforming India into a key provider of global healthcare.

Modern Industry Scale, Export Dominance, and Biotechnology

By 2025/2026, the scale of the Indian pharmaceutical industry had become staggering:

- **Valuation and Scale:** The market is currently valued between $57.6 billion and $60.3 billion, ranking 3rd globally in terms of total production volume.
- **Export Dominance:** India accounts for an astonishing 20% of the total global generic medicine supply by volume, with pharma exports reaching a record $30.47 billion in FY25. Over 60% of these exports supply highly regulated markets including the US, UK, EU, and Japan.
- **US Penetration:** Indian manufacturers supply roughly 40% of all generic drugs consumed within the United States, operating over 600 USFDA-approved facilities—the largest number outside the US itself.
- **Global Health Impact:** The nation proudly supplies over 80% of all antiretroviral (ARV) drugs utilized globally to combat HIV/AIDS and produces an estimated 60% of the world's vaccines.
- **Biotechnology Surge:** The sector is rapidly diversifying into biopharmaceuticals (vaccines, therapeutics, diagnostics) and high-margin biosimilars.

India's Top 20 Pharmaceutical Giants: Leadership, Scale, and Global Footprint: A breakdown of the leading domestic and export-driven pharmaceutical manufacturers headquartered in India, ranked by estimated FY25/FY26 consolidated revenue.

Table 1.4: India's Top 20 Pharmaceutical Giants: Leadership, Scale, and Global Footprint

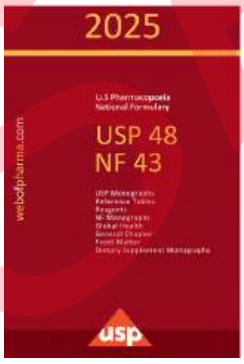
Company	Founder(s)	Primary Product Domain	Global Presence	Est. Revenue (INR)
SUN PHARMA	Dilip Shanghvi	Specialty generics, dermatology, neurology	100+ countries	₹54,729 Cr
AUROBINDO	P.V. Ramprasad Reddy, K. Nityananda Reddy	APIs, finished dosages, neurosciences	150+ countries	₹31,000 Cr
Dr.Reddy's	Anji Reddy	Global generics, biosimilars, APIs	76 countries	₹28,409 Cr
Mankind Pharma Serving Life	Ramesh Juneja, Rajeev Juneja	Consumer wellness, OTC, primary care	Primarily Domestic	₹27,958 Cr
Cipla	K.A. Hamied	Respiratory, anti-retrovirals (ARV), access-care	80+ countries	₹27,547 Cr

Mexican Pharmacopoeia (FEUM)	Mexico	13th Edition / 5.0 Supplement	Permanent Commission of the Pharmacopoeia (CPFEUM)

1.4.4.1 United States Pharmacopeia & National Formulary (USP-NF)

The development of the United States Pharmacopeia began in January 1817 when Dr. Lyman Spalding proposed a unified national standard to the Medical Society of New York. Spalding's initiative divided the United States into four regional districts to draft preliminary standards, which were then consolidated at a General Convention in 1820. This resulted in the publication of the first USP a 272-page volume containing 217 drugs, printed in both English and Latin. Because the USP maintained strict clinical selectivity, only admitting drugs with proven therapeutic value, many widely used preparations were excluded. To address this, the American Pharmaceutical Association (APhA) published the National Formulary of Unofficial Preparations in 1888. Both the USP and the National Formulary (NF) were officially granted legal authority by the Pure Food and Drug Act of 1906, compelling manufacturers to adhere strictly to their chemical and physical standards. The two compendia operated independently until 1975 when they were unified, with the first combined USP XX-NF XV published in 1980.

Transitioning from its historical ten- and five-year revision cycles, the USP-NF is now a highly dynamic, non-governmental public health institution recognized in over 130 countries. As of 2026, the USP-NF operates entirely on a digital platform updated continuously via a rolling annual schedule (e.g., USP-NF 2026 Issues 1 through 6). This modern, online-only infrastructure features advanced Annotation Hubs and real-time revisions, allowing regulatory agencies and pharmaceutical manufacturers instantaneous access to the newest documentary standards, reference materials, and impurity limits without waiting for massive, printed volumes to be released.



1.4.4.2 British Pharmacopoeia (BP)

Pharmaceutical regulation in the United Kingdom holds some of the deepest historical roots, with oversight originating around 1547 when physicians of The Royal College were empowered to inspect and destroy defective apothecary stocks in London. The first regional standard, the London Pharmacopoeia, was published in 1618. For centuries, the UK operated under three distinct city-pharmacopoeias London, Edinburgh, and Dublin until they were amalgamated into the first unified British Pharmacopoeia in 1864. In 1968, the Medicines Act firmly established the statutory authority of the British Pharmacopoeia Commission. Today, the BP is enforced under the Human Medicines Regulations 2012, dictating the legal standards for all medicinal products and active pharmaceutical ingredients sold or supplied in the UK, while also serving as the national standard for countries like Australia and Canada.

The BP 2026, which became legally effective on January 1, 2026, supersedes all previous iterations and stands as a comprehensive global benchmark comprising approximately 4,000 monographs across its six volumes. A defining structural characteristic of the BP is that it reproduces all monographs and requirements of the European Pharmacopoeia (Ph. Eur.) verbatim, rendering it an inherently harmonized text. The 2026 edition introduces 19 completely new UK-specific monographs alongside 34 new monographs adopted from the Ph. Eur., while also providing critical updates to infrared reference spectra and BP Chemical Reference Substances (BPCRS).

1.4.4.3 European Pharmacopoeia (Ph. Eur.)

Emerging much later than its national counterparts, the European Pharmacopoeia was conceptualized in 1964 under the auspices of the Council of Europe. Eight founding nations (Belgium, France, Germany, Italy, Netherlands, Switzerland, Luxembourg, and the UK) signed a convention to unify the varying medicinal specifications across the continent. The first edition was published in 1967. In 1996, the administrative and technical operations were centralized under the newly formed European Directorate for the Quality of Medi-

patient's name, medicine name, dose, frequency, route of administration, duration, storage instructions, date of dispensing, and warning labels such as "Shake well before use," "For external use only," and "Keep out of reach of children."

Figure 1.12: Prescription Handling Process: From Receiving to Compounding, Packaging and Labeling

Container Selection Guidelines:

- **Round vials:** Tablets and capsules.
- **Oval narrow-mouthed bottles:** Low viscosity liquids (mixtures, oral emulsions).
- **Wide-mouthed bottles:** High viscosity liquids, bulk powders, or large quantities of capsules/tablets.
- **Colored fluted bottles:** External preparations (liniments, lotions).
- **Ointment jars / collapsible tubes:** Semisolid dosage forms (creams, ointments).
- **Paper wrappers / envelops:** Oral powders in divided doses.
- **Dropper bottles:** Eye and ear drops.
- **Sifter top containers:** Dusting powders.

(Note: Primary pharmaceutical packaging includes blister packs, ampoules, bottles, sachets, vials, aerosol sprays, and tubes.)

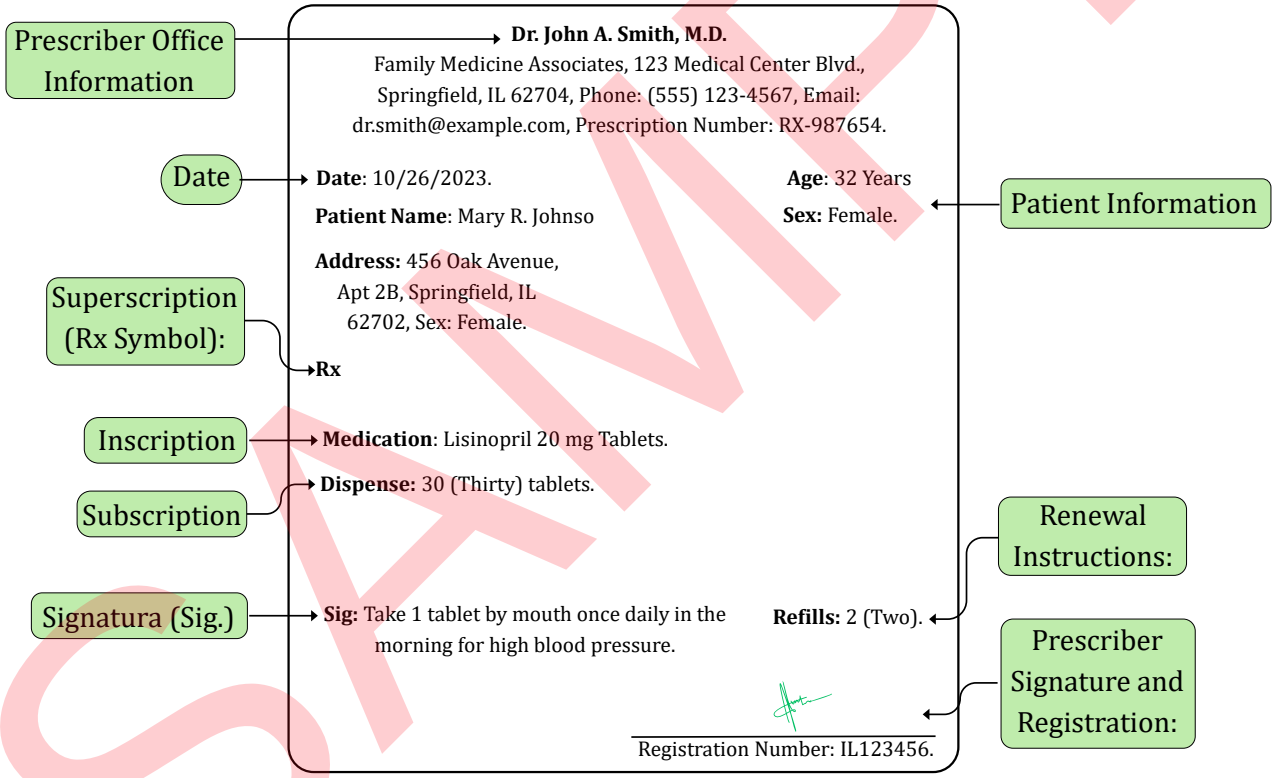


Figure 1.13: Essential Parts of a Prescription: Structure and Key Components

1.5.5 Essential Labelling Requirements

Dispensed medicines require strict labeling to ensure patient safety and compliance.

- **Preparation Name:** Official preparations must use the exact pharmacopoeia name (e.g., PIPERAZINE CITRATE ELIXIR IP), while non-official preparations use the dosage form name (e.g., THE MIXTURE).
- **Strength Information:** Must be specified (e.g., "Each 5ml contains 250mg" or "Each tablet contains 500mg") using whole numbers where possible and placing a zero before decimals.
- **Quantity Supplied:** Total amount must be indicated (e.g., 50ml, 4 tablets).
- **Storage and Expiry:** Temperature, humidity, and light protection details (e.g., "KEEP IN A COOL PLACE" for below 15°C, or "KEEP IN REFRIGERATOR" for 2-8°C).
- **Patient Instructions:** Clear usage directions (e.g., 'One teaspoonful thrice daily'). (Figure 1.18)

SHORT QUESTIONS

1. Define the profession of pharmacy.
2. Mention any four important responsibilities of a pharmacist.
3. Write a short note on the development of pharmacy education in India.
4. What is community pharmacy? State its two major functions.
5. Differentiate between hospital pharmacy and clinical pharmacy.
6. What is industrial pharmacy? Mention the role of pharmacists in pharmaceutical industries.
7. Define pharmacopoeia. Give any four examples of official pharmacopoeias.
8. What is the National Formulary of India?
9. What is an Indian Pharmacopoeia monograph? Mention its major components.
10. Define prescription and list its main parts.

LONG QUESTIONS

1. Explain the profession of pharmacy and discuss its importance in the healthcare system.
2. Describe the history and development of the pharmacy profession in India, with special reference to pharmacy education.
3. Discuss the evolution and major milestones of the pharmaceutical industry in India.
4. Explain the role of important pharmacy organizations in the development of the pharmacy profession in India.
5. Discuss the scope, roles and responsibilities of pharmacists in retail and community pharmacy.
6. Explain the functions and responsibilities of pharmacists in hospital and clinical pharmacy.
7. Describe the scope of industrial pharmacy. Explain the role of industrial pharmacists in manufacturing, quality control, quality assurance and research and development.
8. Define pharmacopoeia. Write a detailed account of the Indian Pharmacopoeia, including its structure, contents and importance.
9. Write detailed notes on IP, BP, USP, BPC and the International Pharmacopoeia.
10. Define prescription. Explain its structure, different parts, importance and proper handling by a pharmacist.

MULTIPLE-CHOICE QUESTIONS

1. The main purpose of the pharmacy profession is to:
(a) Diagnose all diseases
(b) Ensure the safe and effective use of medicines
(c) Perform surgical procedures
(d) Manufacture medical equipment

2. A pharmacist who provides medicines directly to the public generally works in:
(a) Community pharmacy
(b) Forensic laboratory
(c) Veterinary hospital only
(d) Surgical department

3. The pharmacist primarily involved in reviewing and monitoring drug therapy is known as a:
(a) Industrial pharmacist
(b) Clinical pharmacist
(c) Wholesale pharmacist
(d) Medical representative

4. Which of the following is an important responsibility of a community pharmacist?
(a) Conducting major surgery
(b) Patient counselling
(c) Preparing X-ray films
(d) Performing physiotherapy

2 INTRODUCTION TO PHARMACEUTICAL CALCULATIONS & DOSAGE FORMS

- **Introduction:** Metric system of weights and measures; calculations based on alligation, proof spirit, isotonic solutions, dilute solutions (percentage and ratio) and geometric dilution; scientific notation of units and measures.
- **Posology:** Definition and dose calculation based on age, body weight and body surface area.
- **Introduction to Dosage Forms:** Routes of administration and classification of dosage forms.
- **Introduction to Active Pharmaceutical Ingredients and Excipients:** Definition, ideal characteristics and importance

2.1 INTRODUCTION

Metric system of weights and measures; calculations based on alligation, proof spirit, isotonic solutions, dilute solutions (percentage and ratio) and geometric dilution; scientific notation of units and measures.

Pharmaceutical calculations are among the most fundamental skills required in pharmacy practice because they directly influence the safety, quality, efficacy, and therapeutic success of medications. Every pharmaceutical professional, whether involved in drug manufacturing, formulation development, quality control, hospital pharmacy, community pharmacy, or clinical practice, must possess a thorough understanding of pharmaceutical calculations to ensure accuracy at every stage of medication use. Even a minor computational error can result in incorrect drug strength, inappropriate dosage, altered therapeutic outcomes, or serious adverse effects, making mathematical precision an indispensable component of pharmaceutical sciences.

The ability to perform pharmaceutical calculations extends beyond simple arithmetic. It requires an understanding of units of measurement, concentration expressions, dilution principles, and formulation calculations that are routinely applied in pharmaceutical laboratories and healthcare settings. Accurate calculations ensure that formulations are prepared according to pharmacopoeial standards, prescriptions are interpreted correctly, doses are individualized for different patient populations, and medications are compounded safely and effectively. Consequently, competence in pharmaceutical calculations not only enhances professional confidence but also plays a vital role in minimizing medication errors and safeguarding patient health.

A strong foundation begins with the metric system of weights and measures, the internationally accepted system used in pharmaceutical sciences for expressing mass, volume, and length with consistency and precision. Scientific notation of units and measures further simplifies the representation and calculation of extremely large or very small quantities commonly encountered in pharmaceutical analysis, biotechnology, and analytical instrumentation.

Allegation method is a rapid calculation method used to determine the proportions in which two or more ingredients of different strengths must be mixed to obtain a desired concentration. Proof spirit calculations are essential in pharmaceutical and industrial alcohol preparations for determining alcohol strength and performing dilutions according to proof systems.

Calculations involving isotonic solutions are indispensable in the preparation of ophthalmic, parenteral, and nasal formulations, where maintaining osmotic balance is critical to prevent tissue irritation, pain, or cellular damage. Dilute solution calculations, including percentage strength and ratio strength, enable pharmacists to prepare solutions of the required concentration accurately for extemporaneous compounding and routine pharmaceutical preparations. Similarly, geometric dilution provides a systematic technique for achieving uniform mixing of potent drugs with larger quantities of diluents, ensuring dose uniformity and minimizing variability in compounded formulations.

Collectively, these pharmaceutical calculation methods provide the mathematical framework required for accurate formulation, compounding, dispensing, and quality assurance.

- "Proof Strength"=("Percentage strength of alcohol v/v" ×1.753)-100

Proof spirit at a glance:

- 57.1% v/v ethanol = 100° Proof Spirit
- Below 57.1% = Under Proof
- Above 57.1% = Over Proof
- 95% ethanol = Rectified Spirit
- 99.5–100% ethanol = Absolute Alcohol

Example Problems: Proof Spirit

Example 1: Convert 90% v/v alcohol into proof spirit.

Justification: You use the conversion factor derived from the baseline (100 / 57.1) to translate standard percentages into proof degrees.

Calculation:

1. Use the conversion factor: 1 volume of 57.1% v/v alcohol = 100/57.1=1.753 volumes of proof spirit.
2. Multiply your percentage by the factor: 90×1.753=157.77 volumes of proof spirit.
3. This means 100 L of 90% alcohol is equal to 157.77 L of proof spirit.
4. Calculate the O/P value: Because 157.77 is greater than 100, we subtract 100: 157.77-100=57.77 Over Proof (O/P).

The strength is 57.77 Over Proof (O/P).

Example 2: A spirit is labeled as 20° U.P. (Under Proof). What is its actual % v/v strength?

Justification: "Proof" is a baseline of 100. If something is "Under Proof," it means it is below that baseline. You must subtract the U.P. value from 100 to get the actual proof degrees before converting back to percentage.

Calculation:

1. Find actual degrees proof: 100 - 20 (U.P.) = 80 proof.
2. Use the conversion formula: % v/v = (Degrees Proof × 57.1) / 100.
3. Calculate: (80 × 57.1) / 100 = 45.68%.

The spirit is 45.68% v/v.

Example 3: A cask of alcohol is marked 30° O.P. What is its % v/v strength?

Justification: "Over proof" means it exceeds the baseline of 100. You add the O.P. value to 100 to get the working proof value.

Calculation:

1. Find actual degrees proof: 100 + 30 (O.P.) = 130 proof.
2. Use the conversion formula: % v/v = (Degrees Proof × 57.1) / 100.
3. Calculate: (130 × 57.1) / 100 = 74.23%.

The spirit is 74.23% v/v

2.2.5 Isotonic Solutions

Biological membranes (like cell walls) act as selectively permeable membranes, allowing some solvents (like water) to pass through while blocking solutes. The movement of water across this membrane is called osmosis.

Isotonicity: A solution is isotonic with a living cell if there is no net gain or loss of water by the cell when they come into contact.

The Standard: Blood plasma and lachrymal fluid (tears) have the same osmotic pressure as a 0.9% w/v NaCl solution. Therefore, 0.9% NaCl is considered isotonic.

What happens to Red Blood Corpuscles (RBCs) in different solutions? (Figure 2.2)

Isotonic: Osmotic pressure equals 0.9% NaCl. There is no change in shape or size because there is no net movement of water.

Hypotonic: Osmotic pressure is lower than 0.9% NaCl. The cell swells and may burst because water moves from the solution into the cell.

Hypertonic: Osmotic pressure is higher than 0.9% NaCl. The cell shrinks (crenates) because water moves from the inside of the cell out into the solution.

Clinical Importance in Dosage Forms Adjusting tonicity is critical for patient safety and comfort:

Intravenous (IV) & Intrathecal injections: Must be strictly isotonic to prevent RBC hemolysis or disruption of cerebrospinal fluid.

Nasal drops: Must be isotonic to prevent irritation of the

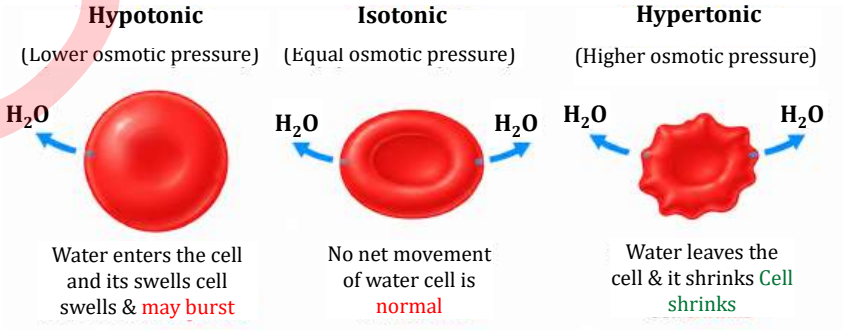


Figure 2.2: Effect of Hypotonic, Isotonic, and Hypertonic Solutions on Red Blood Cells

Thermodynamic temperature	kelvin	K
Amount of substance	mole	mol
Luminous intensity	candela	cd

Although the kilogram is the SI base unit of mass, grams, milligrams, and micrograms are widely used in pharmaceutical calculations and dosage expressions.

Table 2.6: Common Pharmaceutical Units

Quantity	Common units
Mass	kg, g, mg, µg, ng
Volume	L, mL, µL
Length	m, cm, mm, µm, nm
Time	h, min, s
Temperature	°C, K
Amount of substance	mol, mmol, µmol
Concentration	mg/mL, g/L, mol/L
Density	g/mL, kg/m^3
Dose rate	mg/kg, µg/kg/min
Surface area	m^2, cm^2

Table 2.7: Metric Prefixes

Prefix	Symbol	Power of ten	Decimal value
tera	T	10^{12}	1,000,000,000,000
giga	G	10^{9}	1,000,000,000
mega	M	10^{6}	1,000,000
kilo	k	10^{3}	1,000
hecto	h	10^{2}	100
deca	da	10^{1}	10
base unit	—	10^{0}	1
deci	d	10^{-1}	0.1
centi	c	10^{-2}	0.01
milli	m	10^{-3}	0.001
micro	µ	10^{-6}	0.000001
nano	n	10^{-9}	0.000000001
pico	p	10^{-12}	0.000000000001

Purpose and Importance

- Expresses very small drug doses and trace concentrations clearly.
- Expresses extremely large scientific quantities conveniently.
- Reduces the number of written zeros.
- Simplifies multiplication, division, and comparison of magnitudes.
- Makes significant figures more apparent.
- Reduces transcription and calculation errors when used correctly.
- Supports reporting of molecular quantities, microbial counts, particle sizes, and analytical measurements.

2.3.1 Converting Ordinary Numbers into Scientific Notation

a. Numbers greater than 10

Move the decimal point to the left until only one non-zero digit remains before the decimal point. The number of places moved becomes a positive exponent.

$$78{,}500 = 7.85 \times 10^{4}$$

b. Numbers smaller than 1

Move the decimal point to the right until one non-zero digit appears before the decimal point. The number of places moved becomes a negative exponent.

$$0.000072 = 7.2 \times 10^{-5}$$

2.3.2 Converting Scientific Notation into Decimal Form

For a positive exponent, move the decimal point to the right by the number of places indicated by the exponent.

$$3.45 \times 10^{4} = 34{,}500$$

For a negative exponent, move the decimal point to the left by the number of places indicated by the exponent.

$$3.45 \times 10^{-4} = 0.000345$$

Pharmacy-Related Examples

$0.00025\ g = 2.5 \times 10^{-4}\ g = 250\ \mu g$

$0.005\ L = 5 \times 10^{-3}\ L = 5\ mL$

$2{,}500{,}000\ \mu g = 2.5 \times 10^{6}\ \mu g = 2.5\ g$

Multiplication

To multiply values written in scientific notation, multiply the coefficients and add the exponents.

$$(a \times 10^{m})(b \times 10^{n}) = (a \times b) \times 10^{m+n}$$

$$(2.5 \times 10^{3})(4 \times 10^{-2}) = 10 \times 10^{1} = 1.0 \times 10^{2}$$

Division

To divide values written in scientific notation, divide the coefficients and subtract the exponent in the denominator from the exponent in the numerator.

$$(a \times 10^{m}) \div (b \times 10^{n}) = (a \div b) \times 10^{m-n}$$

$$(8 \times 10^{6}) \div (2 \times 10^{2}) = 4 \times 10^{4}$$

Addition and Subtraction

Before addition or subtraction, the powers of ten must be made the same. The coefficients can then be combined.

$$3.2 \times 10^{-3} + 4.5 \times 10^{-4}$$

$$4.5 \times 10^{-4} = 0.45 \times 10^{-3}$$

$$(3.2 + 0.45) \times 10^{-3} = 3.65 \times 10^{-3}$$

Powers

$$(a \times 10^{n})^{m} = a^{m} \times 10^{nm}$$

$$(2 \times 10^{3})^{2} = 2^{2} \times 10^{6} = 4 \times 10^{6}$$

4. The lowest dose at which a drug produces clinically significant toxic effects is known as:
(a) Minimum toxic dose
(b) Minimum effective dose
(c) Loading dose
(d) Prophylactic dose

5. The dosage or concentration range between the MED and MTD is called:
(a) Toxic range (b) Therapeutic window
(c) Lethal range (d) Sub-therapeutic range

6. Which of the following drugs has a narrow therapeutic window?
(a) Amoxicillin (b) Penicillin
(c) Digoxin (d) Cefalexin

7. Which of the following is an example of a drug with a wide therapeutic window?
(a) Lithium (b) Warfarin
(c) Phenytoin (d) Penicillin

8. Therapeutic Drug Monitoring is particularly important for:
(a) Drugs with a narrow therapeutic window
(b) Topical preparations only
(c) Drugs with no systemic action
(d) Nutritional supplements

9. Young's formula is generally used to calculate the dose for children aged:
(a) Below one month (b) 1–12 years
(c) 13–18 years (d) Above 18 years

10. Fried's formula is mainly used for calculating the dose for:
(a) Elderly patients (b) Obese adults
(c) Infants below one year (d) Pregnant women

11. The most accurate method for calculating pediatric doses is based on:
(a) Age alone
(b) Sex
(c) Body Surface Area
(d) Time of administration

12. The Mosteller formula calculates Body Surface Area using:
(a) Age and sex
(b) Height and body weight
(c) Pulse and blood pressure
(d) Dose and dosage frequency

13. Grey baby syndrome in newborns is associated with:
(a) Digoxin (b) Chloramphenicol
(c) Tetracycline (d) Primaquine

14. Compared with an oral dose, the intravenous dose required to produce the same blood concentration is usually:
(a) Higher (b) Equal
(c) Lower (d) Unpredictable in every case

15. Reduced metabolism of morphine may occur in patients suffering from:
(a) Achlorhydria (b) Liver cirrhosis
(c) Iron-deficiency anaemia (d) Bronchial asthma

16. Drug accumulation occurs when:
(a) Drug elimination is faster than absorption
(b) Absorption and elimination are equal
(c) Absorption is slower than metabolism
(d) Drug absorption exceeds drug elimination

17. When the combined effect of two drugs equals the sum of their individual effects, it is called:
(a) Additive effect (b) Antagonistic effect
(c) Idiosyncratic effect (d) Tachyphylactic effect

18. Which of the following solutions is considered isotonic with blood plasma?
(a) 0.45% Sodium chloride (b) 0.9% Sodium chloride
(c) 5% Sodium chloride (d) 10% Sodium chloride

19. Which method is based on freezing point depression for tonicity adjustment?
(a) White-Vincent Method
(b) Sodium Chloride Equivalent Method
(c) Cryoscopic Method
(d) Molecular Distillation Method

20. A solution having a lower osmotic pressure than body fluids is called:
(a) Hypertonic (b) Isotonic
(c) Hypotonic (d) Isohydric

ANSWER KEY

1-b	2-c	3-d	4-a	5-b	6-c	7-d	8-a	9-b	10-c
11-c	12-b	13-b	14-c	15-b	16-d	17-a	18-b	19-c	20-c

3 POSOLOGY

- **Posology:** Definition and dose calculation based on age, body weight and body surface area.

3.1 INTRODUCTION

Posology is a branch of medical science that deals with the dose or quantity of drugs administered to a patient to get the desired pharmacological action. The therapeutic effect of the drugs depends on various factors like age, climate, weight, sex, and so on.

The word Posology is derived from two Greek words "Posos," which means how much, and "logos," which means science. Posology, a part of medicine concerned with drug dosage, is essential to students' curriculum studying medicine and pharmacy. These two important branches of science, namely Medicine and Pharmacy, collectively play an important role in drug prescription and dispensing, where the concepts of Posology come into action.

It is the prescriber's responsibility (Who studied medicine) to prescribe the drugs of adequate amount, strength, and frequency at which the drug is administered. Based on the prescription, it is the responsibility of the pharmacist to check if an overdose of medication has not been prescribed. In a few cases, the pharmacist may advise physicians and other health practitioners on medication selection, dosage, interactions, and side effects.

3.1.1 Pharmacological Parameters and Dose-Response

The fundamental objective of pharmacotherapy is to achieve optimal clinical efficacy while minimizing the risk of adverse, dose-dependent events. Selecting the correct drug dose is one of the most critical responsibilities of healthcare professionals. This delicate balance of rational drug dosing is governed by three core pharmacological metrics: the Minimum Effective Dose (MED), the Minimum Toxic Dose (MTD), and the Therapeutic Window.

Understanding these parameters enables clinicians to prescribe individualized regimens that maximize patient safety and treatment success.

1. Minimum Effective Dose (MED)

The Minimum Effective Dose (MED) is the lowest dose of a pharmaceutical agent required to elicit the desired therapeutic effect in the majority of patients. It marks the threshold at which the drug begins to exert its intended pharmacological action.

Administering a dose below the MED results in an inadequate therapeutic response. At this sub-therapeutic level, the drug concentration fails to reach the minimum threshold required to activate its target receptors or produce sufficient biological activity, leading to treatment failure despite the patient actively receiving the medication.

The MED is not a static, universal value; it fluctuates based on individual patient characteristics, including:

- **Age:** Pediatric and geriatric populations frequently require dose adjustments due to differences in metabolism and body composition.
- **Anthropometrics:** Body weight and body surface area.
- **Biological Sex:** Differences in fat distribution and enzymatic activity.
- **Pharmacogenomics:** Genetic variations affecting drug-metabolizing enzymes.
- **Organ Function:** Hepatic (liver) and renal (kidney) clearance rates.
- **Disease State:** The severity and stage of the underlying pathology.
- **Concomitant Medications:** Drug interactions that may induce or inhibit metabolism.
- **Individual Sensitivity:** Intrinsic physiological variations in how a patient responds to a drug.

Clinical Example: The MED shifts based on disease severity. A patient experiencing severe post-operative pain will require a significantly higher analgesic dose to reach their MED compared to a patient experiencing mild pain, even if both are administered the exact same medication.

Clinical Importance of the MED:

- Prevents underdosing and subsequent therapeutic failure.
- Establishes the recommended starting baseline dose.
- Minimizes unnecessary systemic drug exposure.

- The ratio between the amount of drug administered and body size influences the drug concentration at the site of action.
- Dosage adjustment from the usual adult dose is required for malnourished, obese, or pediatric patients and should be calculated according to body weight.

4. Route of Administration

- Route of administration generally controls the effectiveness of a formulation.
- Intravenous (IV) drugs enter the bloodstream directly, making the whole amount available in the blood. In contrast, oral drugs are rarely fully absorbed due to physical, chemical, and biological barriers (including interactions with gastric and intestinal contents).
- Consequently, a lesser IV injectable dose is required than the oral dose to achieve identical blood levels. The onset of action is quick in IV formulations, carrying a higher chance of drug toxicity.

5. Time of Administration

- Medication administered orally often relates to meals.
- Absorption proceeds more rapidly if the stomach and upper intestinal tract are free of food. A drug effective before a meal may become ineffective if taken during or after eating.
- Drugs causing gastric irritation (iron, arsenic, cod-liver oil) are better tolerated if given after meals to dilute the drug's concentration. Antacid drugs should be taken before meals.

6. Environmental Factors

- Daylight acts as a stimulant, enhancing stimulating drugs and diminishing hypnotics.
- Darkness acts as a sedative, making hypnotics more effective at night. Therefore, the dose of a sedative or barbiturate required to produce sleep during the daytime is much higher than at night.
- Alcohol is better tolerated in winter than in summer.

7. Psychological State

- The psychological state of mind can affect the response to a drug (e.g., a nervous and anxious patient requires more general anesthetics).
- Disorders like angina pectoris and bronchial asthma are known to be cured using placebos. A placebo is an inert dosage form without the active drug that produces therapeutic benefits and is frequently used in clinical trials.
- Women are noted as more emotional than men and might require fewer doses of certain drugs for the desired effect.

8. Pathological States: Several diseases may directly affect therapeutic activity, and doses must be adjusted based on the patient's pathological condition.

- **Achlorhydria:** Reduced gastric secretions (hydrochloric acid) might decrease the absorption of acetylsalicylic acid (Aspirin).
- **Liver Cirrhosis:** Decreases the metabolism of drugs like morphine and pentobarbitone.
- **Fever:** Patients with increased body temperature can tolerate high doses of antipyretics than normal individuals.
- **Kidney Disease:** Diseases affecting filtration and elimination reduce the excretion of drugs like streptomycin, aminoglycosides, digoxin, and phenobarbitone, necessitating lower doses.
- **Regulatory Labeling:** Labels use restrictions like Precautions (advising on possible problems, e.g., fungal overgrowth from tetracycline), Warnings (greater potential for harm, e.g., liver toxicity from tetracycline in renal impairment, indicating lower doses and serum monitoring), and Contraindications (absolute prohibition of drug use under stated conditions).

9. Accumulation

- When a drug's absorption rate exceeds its rate of elimination, it accumulates in the body.
- Drugs with a lower rate of elimination (digitalis, emetine, heavy metals, and chloroquine, which causes retinal damage upon prolonged use) often accumulate and cause toxicity.

10. Drug-Drug Interactions: Concurrent administration of another drug may modify a drug's absorption, distribution, metabolism, or excretion through chemical or physical interaction, producing beneficial or detrimental effects (Table 3.2 & 3.3).

Table 3.2: Relationship Between Administered Drug Dose and Pharmacological Effect

Administered drug dose	Pharmacological effect
Drug A	Effect A
Drug B	Effect B
Drug A + Drug B	Effect AB

Table 3.3: Types of Drug–Drug Interactions with Examples

Drug-Drug interactions	Name of the effect	Examples
Effect ABC = Effect A + Effect B + Effect C	Additive effect	Ephedrine + Aminophylline
Effect AB > Effect A + Effect B	Synergistic effect	Paracetamol + Probenecid
Effect AB < Effect A + Effect B	Antagonistic effect	Histamine + Adrenaline

- **Additive Effect:** Total pharmacological action equals the sum of the individual drugs.

4 INTRODUCTION TO DOSAGE FORMS

- Routes of administration and Classification of dosage forms.

4.1 INTRODUCTION

Pharmaceutical dosage forms are carefully prepared physical forms of medicines in which Active Pharmaceutical Ingredients (APIs) are combined with suitable excipients. They are designed to ensure the safe, effective, and convenient administration of drugs to patients. Dosage forms convert raw drug substances into patient-ready preparations and influence drug delivery, bioavailability, stability, therapeutic effectiveness, adverse effects, and patient compliance. The API is the main chemical component responsible for producing the desired pharmacological action and may be obtained through chemical synthesis, molecular modification, natural sources, or biotechnology.

Excipients are non-medicinal substances intentionally added to pharmaceutical formulations to perform specific functions. They may improve the solubility of poorly soluble drugs, suspend insoluble particles, thicken liquid preparations, dilute potent APIs for accurate dosing, emulsify immiscible liquids, protect drugs from degradation, and prevent microbial growth. Proper selection and proportioning of excipients are essential because they directly affect drug release, formulation stability, manufacturing quality, appearance, taste, and overall patient acceptability.

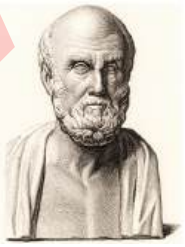
A proper understanding of dosage forms is important for pharmacists because it helps in selecting, dispensing, and counselling patients about medicines correctly. It is also necessary to distinguish between dose and dosage. A dose is the single amount of medicine taken at one time, such as one tablet. Dosage refers to the complete prescribed regimen, including the amount, frequency, and duration of treatment, such as 250 mg twice daily for five days.

4.1.1 Historical Evolution of Dosage Forms

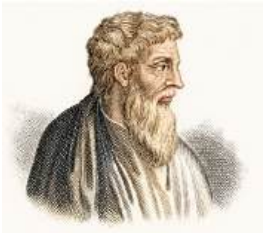
The evolution of pharmaceutical dosage forms represents a fascinating journey through human civilization's quest to deliver therapeutic agents effectively. Ancient civilizations employed crude but effective methods of drug delivery, utilizing natural matrices such as honey, wax, and plant gums to formulate medicinal preparations.

The ancient Egyptians, around 3000 BCE, developed some of the earliest documented pharmaceutical formulations, including pills made from bread crumbs mixed with medicinal substances. The Edwin Smith Papyrus and Ebers Papyrus provide evidence of sophisticated understanding of drug formulation principles, including the use of vehicles and excipients to enhance drug delivery.

Greek and Roman civilizations further advanced pharmaceutical formulation science. Hippocrates (460-370 BCE) described various dosage forms including decoctions, ointments, and pessaries. Dioscorides (40-90 CE) compiled "De Materia Medica," which remained the authoritative pharmaceutical text for over 1,500 years, detailing numerous formulation techniques and dosage forms.



Hippocrates (460–370 BCE)



Dioscorides (40-90 CE)

The medieval period saw significant contributions from Arabian and Islamic scholars. Al-Razi (854-925 CE) and Ibn Sina (980-1037 CE) developed advanced pharmaceutical techniques, including distillation and sublimation methods that influenced European pharmaceutical practice. The concept of controlled-release formulations can be traced to this era, where practitioners used wax matrices to prolong drug release.

Al-Razi (854–925 CE)

Ibn Sina (980–1037 CE)

7. **Company Name/Branding on the Product:** For brand recognition, quality assurance, and patient safety, the inclusion of the company name or product identifier on the dosage form itself (e.g., "Crocin" imprinted on tablets) is a desirable characteristic. This aids in product identification, prevents medication errors, and reinforces brand trust.

4.2 CLASSIFICATION OF ROUTES OF ADMINISTRATION

The route of administration is a critical determinant of a drug's pharmacokinetic profile, influencing its onset, duration, and intensity of action. (Figure 4.2)

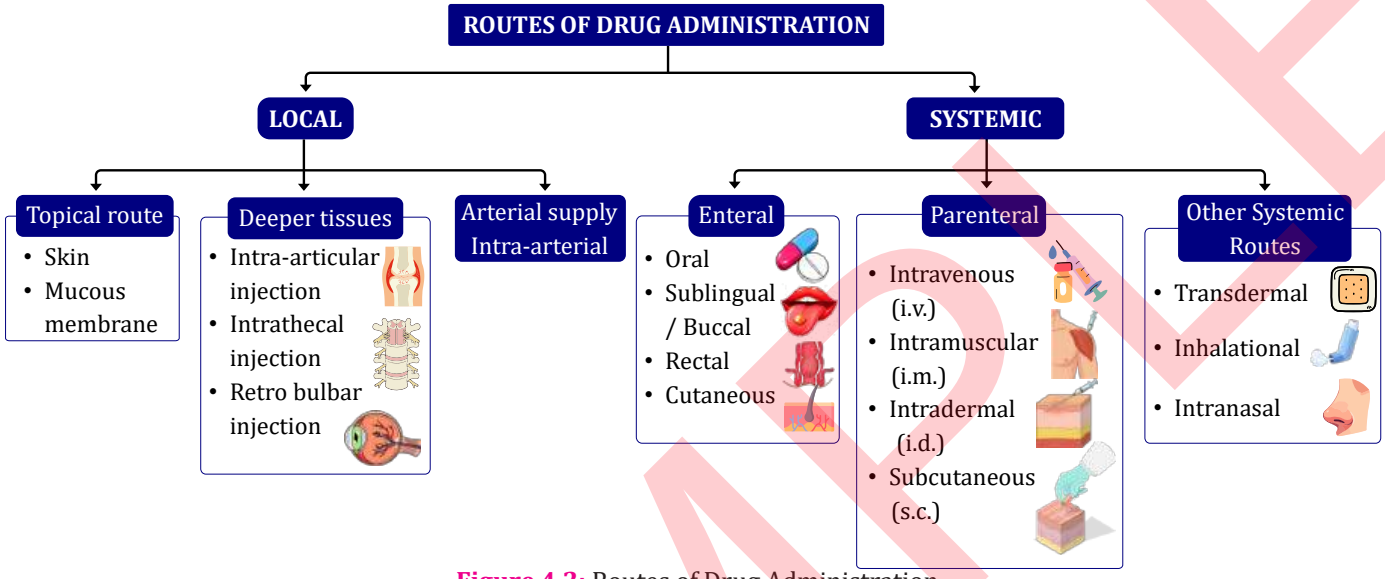


Figure 4.2: Routes of Drug Administration

A. Systemic Routes

I. Enteral Routes

Enteral routes involve administering drugs through the gastrointestinal (GI) tract or oral mucosa. They are the most commonly used routes because they are convenient, safe, non-invasive, and generally well accepted by patients (Table 4.1).

1. Oral Route

The oral route is the most commonly used and convenient method of drug administration. After ingestion, the drug passes through the gastrointestinal tract, where it encounters varying pH conditions, ranging from approximately pH 1–3 in the fasting stomach to pH 7–8 in the colon. During this journey, the drug must overcome biochemical barriers such as gastric acid and digestive enzymes, as well as physical barriers including the mucus layer and intestinal epithelial cells, before absorption can occur. Most orally administered drugs are absorbed from the small intestine and enter the hepatic portal circulation, where they may undergo first-pass metabolism in the liver before reaching the systemic circulation.

Oral dosage forms are prepared using suitable excipients, such as lactose as a filler, crospovidone as a disintegrant, and lubricants to improve manufacturing, dissolution, stability, and drug release. Depending on the therapeutic requirement, oral formulations may be designed as immediate-release, sustained-release, or enteric-coated preparations to protect the drug from gastric acid. The oral route is widely used for both long-term treatment, such as the management of hypertension, and short-term therapy, such as antibiotic treatment, and accounts for a major proportion of marketed medicines (Figure 4.3).

Advantages

1. Convenient and easy to use
2. Enables self-administration
3. Generally safe and economical
4. Suitable for prolonged treatment
5. Available in multiple dosage forms

Limitations

1. Not appropriate for unconscious patients
2. Difficult to use during nausea or vomiting
3. Some drugs may be destroyed by gastric acid or enzymes
4. Drug absorption may be affected by food, pH, and GI movement
5. First-pass metabolism may lower bioavailability

Table 4.1: Summary of Enteral Route

Route	Site of Administration	Onset of Action	Common Dosage Forms	Common Uses
Oral (PO)	Mouth → Stomach → Intestine	Slow (30–90 min)	Tablets, capsules, syrups, suspensions	Most systemic medications
Sublingual (SL)	Under the tongue	Rapid (1–5 min)	Tablets, films, sprays	Nitroglycerin, buprenorphine
Buccal	Between the cheek and gum	Rapid to moderate	Tablets, lozenges, films	Nicotine, fentanyl, hormone preparations
Rectal (PR)	Rectum	Variable	Suppositories, enemas, foams	Antipyretics, laxatives, antiemetics

II. Parenteral Routes

Systemic parenteral routes involve the administration of drugs by injection or infusion directly into the bloodstream or body tissues, completely bypassing the gastrointestinal tract and first-pass metabolism (Table 4.2). These routes provide rapid, reliable, and precise drug delivery, making them essential in emergency care, critical illness, and situations where oral administration is not feasible. Common systemic parenteral routes include intravenous (IV), intramuscular (IM), and subcutaneous (SC) administration (Figure 4.6).

1. Intravenous (IV) Route

The intravenous route involves administering a drug directly into a vein, allowing it to enter the systemic circulation immediately. Veins are composed of three layers the tunica intima, tunica media, and tunica adventitia and the injected drug is rapidly diluted by the circulating blood. Since no absorption process is required, intravenous administration provides an immediate onset of action and 100% bioavailability while completely avoiding gastrointestinal degradation and hepatic first-pass metabolism.

Intravenous preparations must be sterile, pyrogen-free, and free from visible particulate matter. They should preferably be isotonic with blood, approximately 300 mOsm/kg, and maintained within a physiologically acceptable pH range. Single-dose injections are generally formulated without antimicrobial preservatives to minimize the risk of toxicity. The IV route is particularly important during medical emergencies, such as the administration of adrenaline during cardiac arrest, and is also used for delivering large volumes of fluids, total parenteral nutrition, and irritant or cytotoxic drugs used in chemotherapy.

2. Intramuscular (IM) Route

The intramuscular route involves injecting a drug directly into skeletal muscle, which has a rich capillary network that supports efficient absorption into the systemic circulation. The volume that can be administered depends on the injection site; approximately 1–2 mL may be given into the deltoid muscle, while larger muscles in the gluteal region can accommodate up to about 5 mL. Drug absorption through this route is generally faster than subcutaneous administration but slower than intravenous injection. Aqueous solutions provide relatively rapid drug absorption, whereas oily solutions or suspensions may form a depot at the injection site and release the drug gradually over an extended period. The intramuscular route is widely used for vaccines, including hepatitis B and COVID-19 vaccines, as well as depot contraceptives, hormonal preparations, and long-acting antipsychotic medicines that help improve treatment adherence.

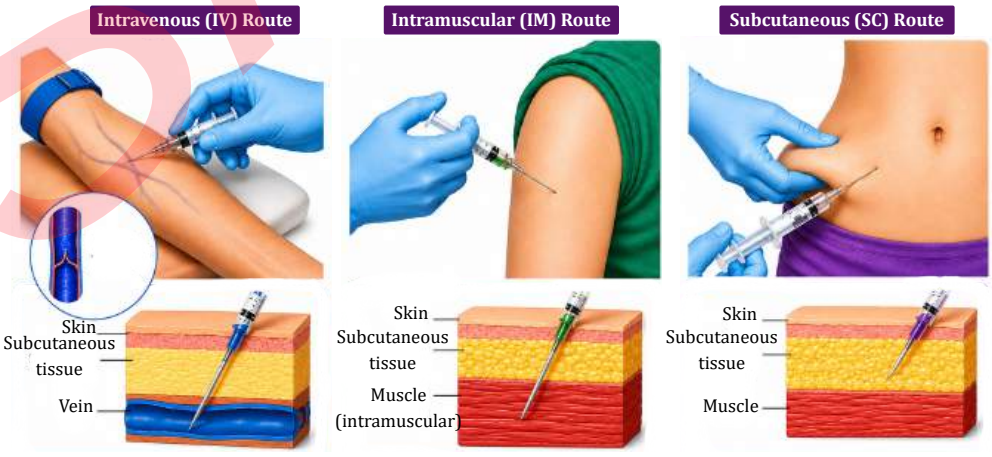


Figure 4.6: Parenteral Routes of Drug Administration

incorrect use can significantly reduce efficacy.

2. **Stability Concerns with Pressurized Systems:** Formulations in pressurized containers require specific stability considerations.
3. **Device Complexity:** Some devices (e.g., nebulizers) can be complex to use and maintain.
4. **Cost:** Often more expensive than conventional oral dosage forms.

Table 4.9 : Marketed Gaseous Dosage Forms

Dosage Form Type	Marketed Examples	Primary Uses & Indications
Aerosols	Tinactin spray	Fine solid/liquid particles suspended in a pressurized gas propellant, providing uniform application over larger topical skin surfaces.
Metered-Dose Inhalers (MDIs)	Ventolin HFA	Pressurized canisters delivering a highly specific, pre-measured dose of aerosol mist straight into the lungs for acute respiratory relief.
Dry Powder Inhalers (DPIs)	Advair Diskus	Device delivering micro-fine dry drug powder directly into the respiratory tract, driven entirely by the patient's own inspiratory effort.
Nebulizers	Pulmicort Respules	Mechanical systems converting liquid solutions into a sustained fine mist inhaled via a mask; optimized for pediatric or severe emergency respiratory distress.

4.3.2 Classification by Release Profile

Classification by Release Profile classifies dosage forms according to the rate and pattern at which the active pharmaceutical ingredient is released after administration. The release profile plays a crucial role in determining the onset, intensity, and duration of a drug's therapeutic effect. By controlling drug release, pharmaceutical formulations can improve treatment efficacy, reduce dosing frequency, minimize adverse effects, and enhance patient compliance. Based on their release characteristics, dosage forms are commonly classified into Immediate Release (IR), Modified Release (MR), Delayed Release (DR), Extended Release (ER), Sustained Release (SR), Controlled Release (CR), and Targeted Release (TR) systems. (Figure 4.12)

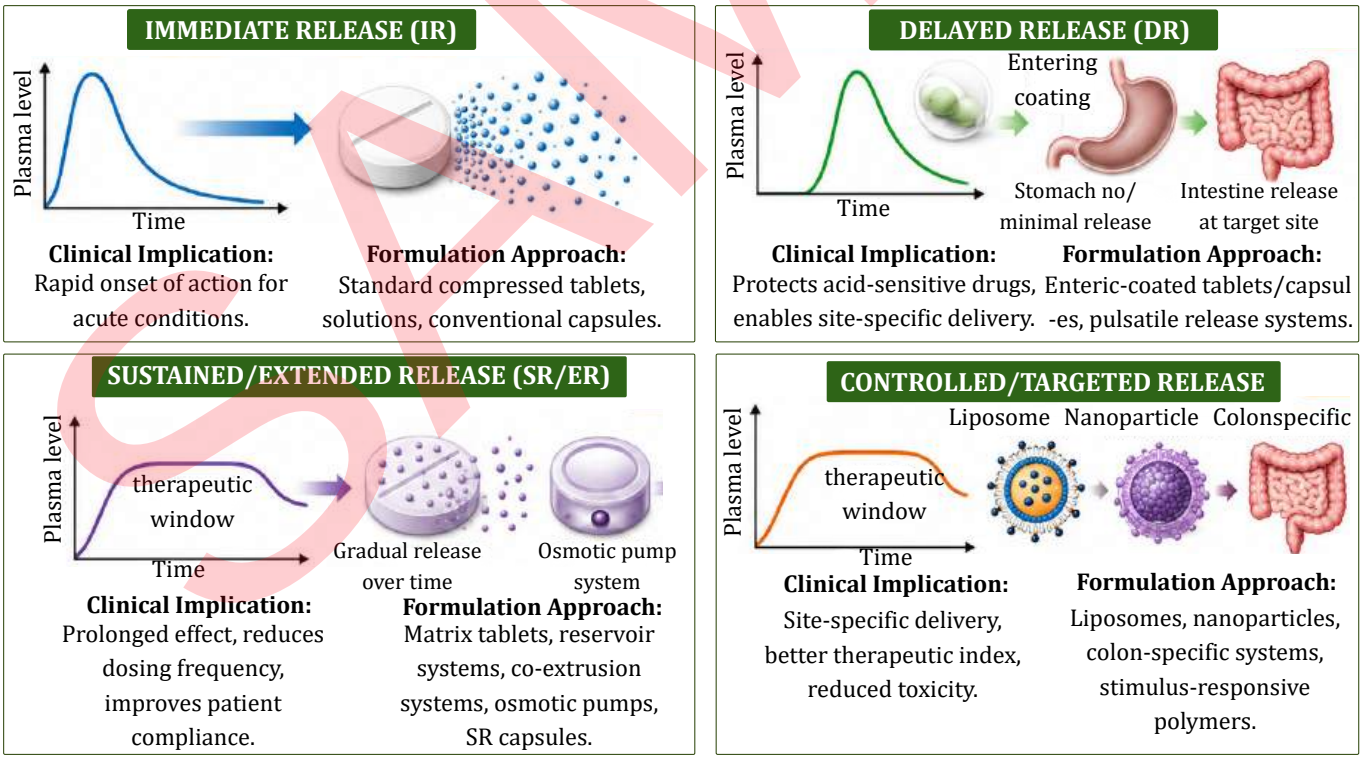


Figure 4.12: Classification By Release Profile

5 INTRODUCTION TO ACTIVE PHARMACEUTICAL INGREDIENTS & EXCIPIENTS

- Definition, ideal characteristics and importance

5.1 INTRODUCTION

In pharmaceutical sciences and regulatory affairs, understanding the distinction between the active and inactive components of a dosage form is foundational.

- **Active Pharmaceutical Ingredient (API):** Often called the "Drug Substance," an API is the chemical or biological substance intended to provide pharmacological activity or a direct effect in diagnosing, treating, or preventing a disease. One can think of the API as the "engine" of the therapeutic effect.
- **Excipients (Inactive Ingredients):** These are all components in a drug product other than the active ingredient. While historically viewed as "inert" fillers, excipients are the "vehicles" that enable drug delivery, stabilize the formulation, and assist in manufacturing.

Table 5.1: Regulatory Difference between API and Excipients

Feature	Active Pharmaceutical Ingredient	Excipient
Primary Definition	Substance intended to furnish pharmacological activity or direct effect (ICH Q7/FDA).	Any component of a drug product other than the active ingredient (IPEC/FDA).
Regulatory Mission	Deliver intended therapeutic effect in treatment or diagnosis.	Aid drug delivery, enhance stability, or assist in processing and identification.
Mass Contribution	Typically present at much lower mass than excipients (potency-driven).	Often comprises the bulk of the dosage form mass; often complex mixtures.
GMP Requirement	High intensity; must strictly comply with ICH Q7 (Drug Substance) standards.	Must comply with compendial monographs or justified specifications (IPEC GMP).

5.2 CHARACTERISTICS OF API's AND EXCIPIENTS

5.2.1 Ideal Characteristics of APIs

APIs must be carefully characterized and controlled to ensure safety and efficacy. Critical Quality Attributes (CQAs) for APIs include:

- **Chemical Purity and Impurity Profile:** APIs must be of high chemical purity, with well-characterized and controlled impurities. ICH Q3A/B guidelines require reporting and qualification of organic, inorganic, and residual solvent impurities. Regulatory texts emphasize that APIs "meet the quality and purity characteristics that they purport… to possess.". A complete impurity profile is established via stability studies and synthetic-process knowledge. Typical tests include HPLC (for organic impurities), GC (for solvents), and ICP-MS (for elemental impurities).
- **Solid-State Form (Polymorphism/Crystals):** Many APIs can exist in multiple solid forms (polymorphs, hydrates, solvates, amorphous forms). ICH Q6A notes that "differences in these forms could… affect quality or performance" and requires that any polymorphic form affecting the product be identified and controlled. For example, carbamazepine, ritonavir, and other APIs have known polymorphs with different solubility or stability. Ideal APIs have a single stable polymorph selected as the product form. Characterization uses X-ray powder diffraction (XRPD), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), and spectroscopic methods to detect polymorphs. Control strategies include salt or co-crystal formation, seeding during crystallization, or solid dispersion techniques to maintain the desired form.

logical activity of natural products with the advantages of synthetic chemistry, such as improved stability, potency, or bioavailability.
Example: Amoxicillin, Ampicillin, Hydromorphone.

C. Biologically Derived APIs

Biologically derived APIs are obtained from living organisms, including microorganisms, plants, and animal cells. They are produced using fermentation, cell culture, or extraction techniques and possess complex molecular structures with high biological specificity. These APIs are widely used in biotechnology and biopharmaceuticals.
Example: Insulin, Monoclonal antibodies, Vaccines.

2. Classification by Molecular Nature

Based on their molecular size and structure, APIs are classified into small molecules, peptides, and proteins. Their molecular nature determines their pharmacological properties, stability, manufacturing process, and formulation requirements.

A. Small Molecule APIs

Small molecule APIs are low molecular weight compounds that can easily cross biological membranes. They are generally synthesized by chemical methods and are known for their high stability, oral bioavailability, and economical large-scale production.
Examples: Aspirin, Ribavirin, Metformin.

B. Peptide APIs

Peptide APIs consist of short chains of amino acids (generally fewer than 50 amino acids). They provide high target specificity but are often susceptible to enzymatic degradation, requiring specialized formulation and delivery systems.
Examples: Oxytocin, Glucagon, Liraglutide.

C. Protein APIs

Protein APIs are large, complex biomolecules composed of long amino acid chains with specific three-dimensional structures. They are usually produced by recombinant DNA technology or cell culture and are widely used in treating chronic and complex diseases.
Examples: Insulin, Erythropoietin (EPO), Monoclonal antibodies (e.g., Trastuzumab).

3. Classification by Potency

Based on their pharmacological potency, APIs are classified into Highly Potent APIs (HPAPIs) and Generic APIs. Potency refers to the amount of an API required to produce a desired therapeutic effect. This classification is important for determining dosage, manufacturing requirements, safety measures, and clinical applications.

A. Highly Potent APIs (HPAPIs)

Highly Potent APIs (HPAPIs) produce the desired therapeutic effect at very low doses. Because of their high biological activity, they require specialized manufacturing facilities, containment systems, and strict safety protocols to prevent operator exposure and ensure accurate dosing. HPAPIs are widely used in oncology, hormone therapy, and targeted drug delivery.
Examples: Paclitaxel, Doxorubicin, Tamoxifen.

B. Generic APIs

Generic APIs are active pharmaceutical ingredients used in generic medicines after the patent of the original drug has expired. They possess the same quality, strength, safety, and efficacy as the reference (innovator) product but are manufactured by different companies. Generic APIs are produced on a large scale, making medicines more affordable and widely accessible.
Examples: Paracetamol, Metformin, Atorvastatin.

5.4.2 Excipient

Modern pharmacy recognizes the "functional activity" of excipients; they are not just dead weight. If an excipient significantly enhances drug absorption, it can effectively alter how a drug performs in the body, which requires rigorous safety justification to regulatory agencies like the FDA or EMA (Figure 5.1).

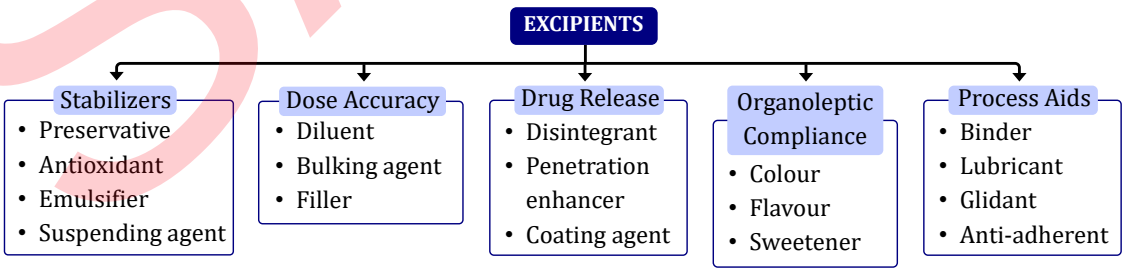


Figure 5.1: Classes of Excipients used in Drug Formulations

1. ORGANOLEPTIC AGENTS

Colours

Colouring agents are substances added to pharmaceutical dosage forms to improve appearance, identify medicines,

6 POWDERS

- **Powders:** Classification, advantages and disadvantages; dusting powders, effervescent powders, efflorescent powders, hygroscopic powders and eutectic mixtures; introduction to excipients and methods of preparation.

6.1 INTRODUCTION

Powders represent one of the oldest, most fundamental, and highly versatile dosage forms in pharmaceutical sciences. They are structurally defined as intimate mixtures of dry, finely divided active pharmaceutical ingredients (APIs) and/or chemicals intended for internal or external administration. Formulations may contain a single API or a combination of multiple drugs, along with appropriate pharmaceutical excipients designed to enhance manufacturability, stability, and patient acceptability.

Historically, powders were the predominant dosage form prior to the widespread adoption of modern tablets and capsules, primarily because they allowed for easy preparation, accurate weighing, and convenient dispensing. Despite the evolution of pharmaceutical technology, powders maintain a critical role in modern therapeutics. This enduring relevance is due to their formulation flexibility, inherent stability, economical manufacturing processes, and broad applicability across various routes of administration.

Furthermore, powder technology forms the foundational basis for industrial pharmacy, as powders function as critical intermediates in the manufacturing of tablets, capsules, pellets, granules, and advanced novel drug delivery systems. The therapeutic efficacy of these formulations is heavily dependent on physicochemical properties, including particle size, size distribution, shape, surface area, porosity, density, flowability, compressibility, moisture content, hygroscopicity, and electrostatic behavior. These properties collectively dictate manufacturing feasibility, dissolution rates, bioavailability, content uniformity, and ultimately, patient compliance.

The Need for Powders as a Pharmaceutical Dosage Form

Powders remain a fundamentally indispensable dosage form in modern therapeutics because they successfully fulfil numerous pharmaceutical and clinical requirements. The rationale for formulating drugs as powders includes the following critical factors:

- **Improved Chemical Stability:** Many pharmacological agents are highly susceptible to hydrolysis and rapid degradation when formulated or stored in aqueous solutions. Formulating these active ingredients as dry powders significantly prolongs their shelf life by minimizing their exposure to moisture. Notable examples include Amoxicillin Dry Syrup, Cefixime Dry Syrup, Ceftriaxone Injection, and Meropenem Injection. Furthermore, dry formulations protect drugs against microbial growth and oxidation during storage.
- **Faster Drug Dissolution and Absorption:** Fine powder particles inherently possess a much larger surface area compared to solid, compressed dosage forms like tablets or capsules. According to the principles of the Noyes–Whitney equation, this increased surface area directly results in faster dissolution rates in biological fluids. This rapid dissolution leads to rapid absorption and a consequently quicker onset of therapeutic action, as seen in preparations like ORS Powder, ENO Fruit Salt, and various antacid powders.
- **Flexible Dose Adjustment:** Unlike tablets and capsules which contain rigidly fixed doses, powders allow for highly individualized dose adjustments. This flexibility is particularly useful and critical in pediatrics, geriatrics, oncology, veterinary practice, and the broader field of personalized medicine.
- **Suitability for High-Dose Drugs:** Drugs that require large volumetric doses are notoriously difficult or impossible to formulate into manageable tablets or capsules. However, they can easily be dispensed and consumed as powders. Examples of such high-dose formulations include Isabgol Husk, protein powders, electrolyte powders, and large-dose antacid powders.
- **Ease of Administration:** Powders can be seamlessly mixed with vehicles such as water, milk, fruit juice, or food immediately prior to administration. This makes them highly suitable for patients who have difficulty swallowing solid solids, such as young children, the elderly, dysphagic patients, and patients utilizing feeding tubes.

ing and geometric dilution in a mortar ensures the even mixing of active drugs and inert diluents.

4. **Sieving:** This process involves passing bulk powders through standardized screens or sieves (frequently mesh No. 80–100).
- Sieving systematically breaks apart agglomerates and lumps, ensuring a uniformly distributed particle size.
- It is routinely employed both before and after the blending phases of manufacturing.

5. **Wet Granulation:** This is a comprehensive, large-scale production method utilized to convert fine powders into free-flowing, compressible granules.
- First, the active pharmaceutical ingredient and excipients are blended dry.
- A liquid binder solution (e.g., Povidone/PVP in water) is subsequently added while mixing to wet the particles and form a cohesive damp mass.
- This wet massing is then forced through a granulator machine to create wet granules.
- The granules are dried gently using tray dryers or fluid-bed dryers, and then sieved once more to remove overly fine particles or large lumps.
- Finally, a lubricant or glidant is blended with the dried granules as a terminal step.

6. **Dry Granulation:** This technique is exclusively reserved for moisture-sensitive materials that would degrade in wet granulation.
- Dry powders are directly compacted under high pressure by slugging (punching the powder into very large, crude tablets) or through continuous roller compaction.
- The resulting solid compacts are then mechanically milled back down into uniform, free-flowing granules.

7. **Fusion (Eutectic) Method:** Used predominantly to prepare eutectic mixtures or specific suppository bases.
- Components are physically melted together (provided their degradation temperatures allow) and allowed to solidify.
- The solidified mass is subsequently ground into a fine powder.
- In a modified dry blending fusion process for effervescent granules, powdered acids and carbonates are mixed at low temperatures under strict desiccation to avoid premature chemical reactions.

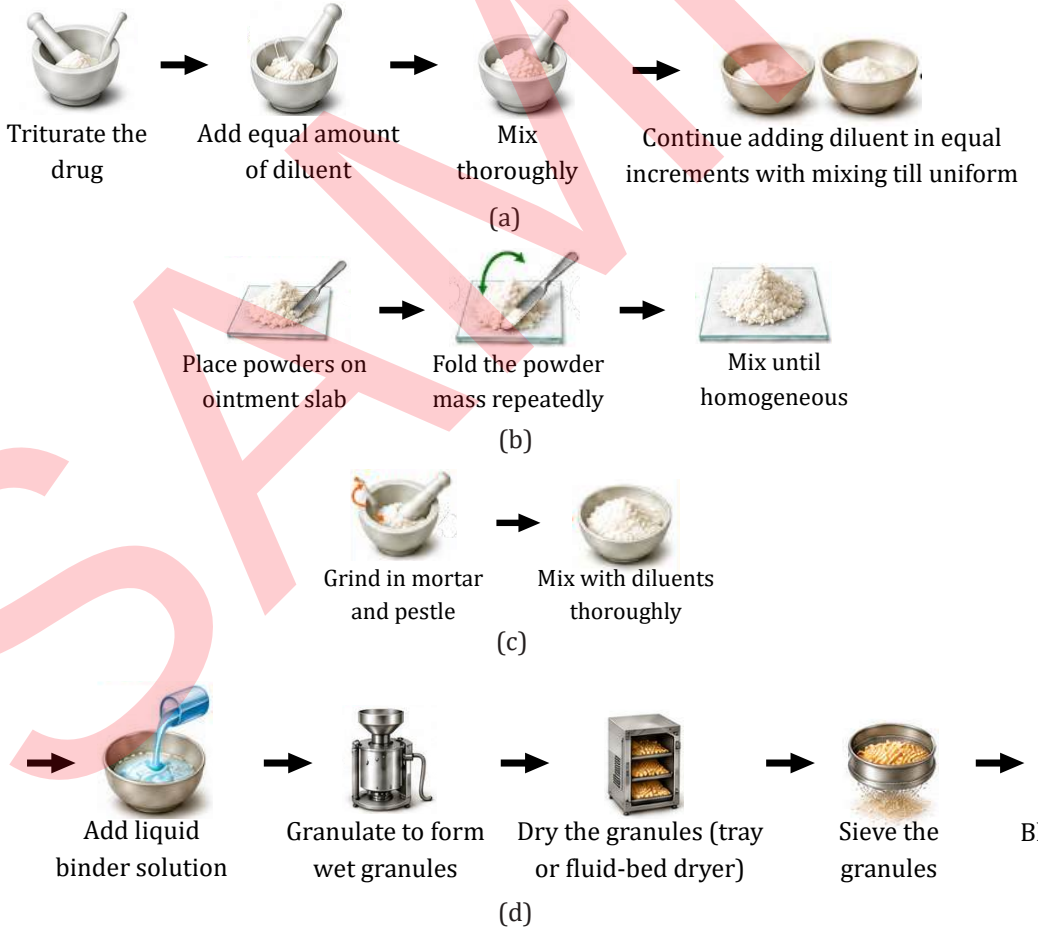


Figure 6.3 : Methods of Preparation:(a) Geometric Dilution; (b) Spatulation; (c) Trituration; (d) Wet Granulation

ic percentile limits, commonly denoted as d_10, d_50, and d_90 :

- **d_{10}:** The equivalent spherical diameter at which 10% of the sample's total mass or volume is comprised of smaller particles.
- **d_{50}** (Median Particle Diameter): The precise median diameter separating the cumulative distribution into two statistically equal halves; exactly 50% of the material resides above this dimension and 50% below it.
- **d_{90}:** The equivalent diameter at which 90% of the sample consists of particles smaller than this value.

For practical, industrial categorization, particularly where mechanical sieving is employed for bulk fractionating, powders are broadly classified according to the nominal mesh aperture through which a specified percentage of the material successfully passes.

Standard Pharmacopeial Powder Categories

The traditional classification system is determined by a combination of the maximum sieve opening through which all particles pass and a secondary minimum sieve opening defining the permitted retention of finer particles, establishing the optimal d_50 range. The descriptive terminology and standard sieve opening equivalents are summarized in the following table (Table 6.7).

Table 6.7 : Standard Pharmacopeial Powder Categories

Descriptive Classification	Particle Dimension Requirement & Nominal d50 Range	Primary Sieve Equivalent (Nominal Aperture)	Secondary Retention Sieve Requirement
Very Coarse	>1000 µm	> 1000 µm (No. 18)	-
Coarse	All pass 2000 µm (No. 10), ≤40% pass 355 µm; d_50 range: 355–1000 µm	2000 µm (No. 10)	No. 44 (355 µm)
Moderately Coarse	All pass 710 µm (No. 22), ≤40% pass 250 µm	710 µm (No. 22)	No. 60 (250 µm)
Moderately Fine	All pass 355 µm (No. 44), ≤40% pass 180 µm; d_50 range: 180–355 µm	355 µm (No. 44)	No. 85 (180 µm)
Fine	All pass 180 µm (No. 85); d_50 range: 125–180 µm	180 µm (No. 85)	-
Very Fine	All pass 125 µm (No. 120); d_50 range: 90–125 µm	125 µm (No. 120)	-
Microfine	≥90% passes 45 µm by weight	45 µm (No. 325)	-
Superfine	≥90% (by number) <10 µm	<10 µm (Requires microscopy/diffraction)	-

These classifications provide formulators with an immediate macroscopic assessment of the material. For instance, coarse powders are generally utilized as bulk intermediates or aggregate classifications. Moderately fine powders represent ideal target size ranges for free-flowing granulation, while very fine to superfine micro-powders are absolutely essential for the formulation of stable colloidal suspensions, topical dusting powders, or dry powder inhalants.

6.11.2 Advanced Particle Size and Size Distribution Analysis

Particle size in a bulk pharmaceutical lot is rarely monodispersed (where all particles possess the exact same diameter). Instead, pharmaceutical powders are inherently polydisperse or heterodisperse, requiring sophisticated statistical distributions to represent the continuum of varying particle dimensions accurately. Furthermore, the precise measurement of these physical dimensions depends entirely on the specific physicochemical property exploited by the analytical instrument such as physical volume, scattered light intensity, terminal sedimentation velocity, or aerodynamic inertia.

I. Analytical Sieving and Advanced Sieve Calibration

Mechanical sieving remains the most prevalent, historically robust, and pharmacopeially endorsed macroscopic technique for estimating the mass-weighted particle size distribution of bulk powders. It is generally indicated for formulations where at least 80% of the constituent particles are larger than 75 µm.

a. Analytical Sieving

Analytical sieving is a method used to determine the particle size distribution of dry powders. A stack of standard sieves is arranged with the largest mesh opening at the top and the smallest at the bottom, ending with a collection pan. A known weight of powder (usually 100 g) is placed on the top sieve, and the stack is shaken mechanically for 5–10 minutes.

7 TABLETS

- Definition, types of tablets including moulded tablets and pills with examples; advantages and disadvantages; introduction to excipients and methods of preparation.

7.1 INTRODUCTION

Tablets are the most widely used solid dosage forms, accounting for nearly 70–80% of pharmaceutical products because of their convenience, accurate dosing, stability, ease of administration, and cost-effectiveness. They contain one or more Active Pharmaceutical Ingredients (APIs) along with suitable excipients that facilitate manufacturing, improve stability, enhance appearance, and ensure proper drug release.

Most tablets are administered orally and are manufactured by compression of powders or granules, although some are prepared by moulding. Depending on the formulation, tablets may provide immediate or modified drug release and are available in various specialized forms, such as chewable, effervescent, dispersible, sustained-release, enteric-coated, and orally disintegrating tablets. Their precision, stability, and economical production make them the preferred dosage form in pharmaceutical practice.

Components of a Tablet

Every tablet contains two major components:

a. Active Pharmaceutical Ingredient (API): The API is the chemical substance responsible for producing the desired therapeutic effect. Examples include:

- Paracetamol in Paracetamol tablets
- Metformin in Metformin tablets
- Diclofenac sodium in Diclofenac tablets

b. Pharmaceutical Excipients: Excipients are inactive substances that assist in manufacturing and improve the quality of tablets. Common excipients include:

- Diluents
- Binders
- Disintegrants
- Lubricants
- Glidants
- Colouring agents
- Flavouring agents
- Sweetening agents

Definitions of Tablets

Different pharmacopoeias define tablets in slightly different ways; however, the fundamental concept remains the same.

According to the Indian Pharmacopoeia (IP)

"Pharmaceutical tablets are solid, flat or biconvex unit dosage forms prepared by compressing one or more drugs, with or without suitable diluents and excipients."

According to the Indian Pharmacopoeia, tablets are solid dosage forms containing one or more active drugs, usually flat or biconvex in shape, prepared mainly by compression, with excipients added as necessary to facilitate manufacture and improve product quality.

According to the United States Pharmacopeia (USP)

"Tablets are solid dosage forms containing medicinal substances with or without suitable pharmaceutical excipients, prepared by compression or moulding."

According to the United States Pharmacopeia (USP), tablets are solid unit dosage forms containing one or more medicinal substances, manufactured by compression or moulding, and formulated with suitable excipients to improve physical properties, stability, and patient acceptability.

7.2 TYPES OF TABLETS

(a) Tablets Ingested Orally

Tablets ingested orally are solid unit dosage forms intended to be swallowed through the mouth, where they disintegrate or dissolve in the gastrointestinal (GI) tract to release the active pharmaceutical ingredient (API) for local or systemic therapeutic action. They are the most widely used pharmaceutical dosage form because they provide accurate dosing, excellent chemical and physical stability, ease of manufacturing, portability, and cost-effectiveness. These tablets are generally administered with water (except chewable tablets), and they may be manufactured by compression or molding techniques. Depending on the formulation,

stomach fluids from entering the tablet (ruining dissolution) and prevents particles from bonding (resulting in soft, fragile tablets).

c. Applications

i. **Mandatory Extragranular Addition:** Lubricants must be added exclusively during the absolute final blending phase, physically dusting the external surface of the completed granules right before they enter the press hopper.

ii. **Strict Blending Parameters:** Blending times are critically validated and deliberately brief (typically capped at 2 to 5 minutes) using extremely low mechanical shear. This prevents the hydrophobic lubricant from forming a continuous, waterproof film that would destroy tablet dissolution.

iii. **Concentration Optimization:** Used only in microscopic quantities to carefully balance manufacturing speed against therapeutic bioavailability. Typical concentrations range strictly from 0.25% to 2% w/w.

Table 7.4: Examples of Lubricants

Excipient Example & Brand Names	Classification	Application
Magnesium Stearate (Ligamed, Magnesia)	Hydrophobic (Metallic Salt of Fatty Acid)	The undisputed gold standard of boundary lubricants, offering unparalleled efficiency at low concentrations (0.25–1%). However, it is highly sensitive to over-blending (causing waterproofing and soft tablets). Its alkaline nature renders it chemically incompatible with highly acidic drugs (e.g., aspirin), catalyzing their degradation.
Sodium Stearyl Fumarate (SSF) (Pruv, Kolliwax SSF, Farmal SSF)	Hydrophilic (Fumaric Acid Monoester)	A highly engineered, water-soluble alternative to magnesium stearate. Because it contains a highly polar functional group, it does not impede water ingress into the tablet, meaning it rarely slows down disintegration. Crucially, SSF is completely insensitive to over-blending, offering immense manufacturing flexibility.
Stearic Acid	Hydrophobic (Saturated Fatty Acid)	A naturally derived fatty acid acting as a moderate boundary lubricant. It is heavily preferred when metallic ions (like the magnesium in magnesium stearate) catalyze chemical incompatibilities or oxidation with the active drug.
Calcium Stearate	Hydrophobic (Metallic Salt of Fatty Acid)	Acts similarly to magnesium stearate but is less commonly used; occasionally selected when magnesium ions present specific incompatibilities with the API.
Hydrogenated Vegetable Oil (Sterotex, Lubritab)	Hydrophobic (Lipid)	Utilized as an alternative hydrophobic lubricant when metallic stearates are inappropriate. It provides good boundary lubrication but must be carefully controlled to prevent delayed dissolution.

B. Glidants

Glidants are finely divided, dry powder additives specifically designed to optimize and radically enhance the bulk flowability of a particulate blend. They reduce inter-particulate friction and cohesive forces, ensuring that the powder flows freely and uniformly from the storage hopper into the die cavity of the tablet press.

a. Classification

Glidants are largely classified by their chemical makeup:

i. **Inorganic Silicas & Silicates:** Colloidal Silicon Dioxide, Magnesium Silicate.

ii. **Minerals:** Talc.

iii. **Organics:** Corn Starch (used at lower concentrations for flow).

b. Functions and Roles

i. **Microscopic Sp acers (Reducing Friction):** Pharmaceutical powders are often highly micronized and possess massive static and van der Waals cohesive forces, causing them to clump together. Nanoscale glidant particles aggressively adhere to the surface of the larger drug granules, acting as physical spacers that push the granules slightly apart, exponentially dropping attractive forces.

ii. **Surface Smoothing (Filling Asperities):** Granules are inherently rough and irregular under a microscope. Glidant nanoparticles physically fall into the microscopic "craters" and asperities on the surface of the host granules. This rounds out the granules, making them perfectly smooth and spherical like microscopic ball bearings, allowing them to flow flawlessly.

iii. **Moisture Scavenging:** Humidity causes sticky liquid bridges to form between particles, halting powder flow. Potent glidants act as aggressive desiccants, sucking up ambient trace moisture and keeping the powder bone-dry and fluid.

Coating Agents (Polymers)	Protects the core, masks tastes, or provides specialized, targeted release profiles (enteric, sustained).	HPMC (Opadry, Methocel), Cellulose Acetate Phthalate (Cellacefate), Ethylcellulose (Surelease).
Coating Agents (Plasticizers)	Lowers the glass transition temperature (T_g) of the polymer film to drastically increase elasticity.	Polyethylene Glycol (PEG), Triethyl Citrate, Propylene Glycol.
Coating Agents (Opacifiers)	Shields the API from photolytic UV degradation by rendering the polymer film completely opaque.	Titanium Dioxide (TiO_2).
Sweeteners	Masks the bitter taste of raw APIs, drastically increasing pediatric/geriatric patient compliance.	Sucralose (Splenda), Aspartame (NutraSweet, Equal), Saccharin (Sweet'N Low), Mannitol, Stevia (Truvia).
Flavoring & Coloring Agents	Enhances aesthetic appeal, masks olfactory odor, and ensures critical brand and dose identification.	Enhances aesthetic appeal, masks olfactory odor, and ensures critical brand and dose identification.

7.4.2 Methods of Tablet Preparation

Unprocessed pharmaceutical powders frequently exhibit poor micromeritic properties, specifically erratic flowability and poor compressibility.

To optimize these powders for high-speed manufacturing, formulators often employ granulation, a process of particle size enlargement wherein fine primary particles are coerced into adhering to one another to form larger, multiparticulate entities. This process standardizes bulk density, ensures uniform powder flow into the machine dies, and facilitates mechanical interlocking and plastic deformation during compression (Figure 7.4).

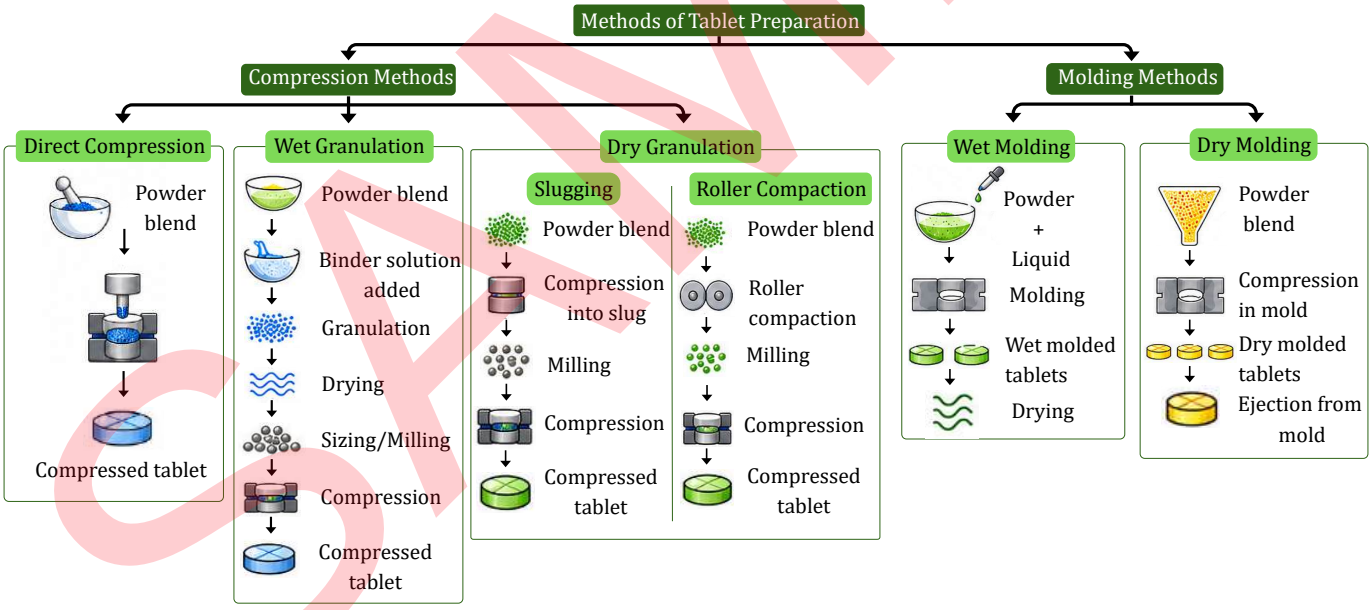


Figure 7.4: Methods of Preparation of Tablets

7.4.2.1 Compression Methods

Compression relies on the application of mechanical force to a powder bed within a die cavity, inducing elastic and plastic deformation, as well as particle fragmentation, to yield a coherent solid compact.

1. Direct Compression: Direct compression is the simplest and most efficient tablet manufacturing method because it eliminates the granulation and drying steps. In this process, the active pharmaceutical ingredient (API) is uniformly blended with directly compressible excipients and the mixture is fed directly into the tablet press for compression. This method requires that the formulation components possess excellent flowability and compressibility; therefore,

8 CAPSULE DOSAGE FORM

- Definition, types of capsules, advantages and disadvantages, capsule sizes; introduction to excipients and methods of preparation.

8.1 INTRODUCTION

Capsules are solid oral dosage forms in which one or more medicaments are enclosed within a water-soluble, biodegradable hard or soft shell. The shell is typically made from gelatin, which provides a simple, easy-to-swallow formulation that generally does not require any additional coating steps.

Need and Rationale for Capsules as a Dosage Form

The development and widespread use of capsules are driven by several therapeutic, manufacturing, and patient-centric needs:

1. **Patient Acceptability:** Consumers widely welcome capsules because their elegant appearance, shape, and smooth, slippery texture make them very easy to swallow and handle.
2. **Taste and Odor Masking:** The tasteless, physiologically inert shell effectively hides the unpleasant taste, color, and odor of active pharmaceutical ingredients.
3. **Enhanced Bioavailability:** Capsule formulations often provide better bioavailability and a faster onset of action compared to standard compressed tablets. Softgels are especially valuable for this, as they can deliver poorly water-soluble drugs in a liquid solution or microemulsion, vastly improving absorption.
4. **Formulation Flexibility:** Hard capsules allow formulators to use a wide variety of excipients—ranging from dry solids to non-aqueous solutions—without subjecting the materials to the high compression stress required for tableting.
5. **Modified and Targeted Release:** Capsules can be tailored to achieve rapid, controlled, or modified release profiles, and can be formulated to deliver drugs to specific sites along the gastrointestinal tract or to the lungs.
6. **Drug Stability:** Capsule shells can be opacified to protect sensitive contents from light, while lipophilic softgel systems can protect drugs from oxidation, photodegradation, and hydrolysis.
7. **Manufacturing Safety:** Encapsulating highly potent or cytotoxic drug compounds into softgels or liquids reduces hazardous powder dust, providing a safer handling environment for manufacturing operators.
8. **Dose Uniformity:** Liquid-filled capsules provide excellent and precise dose uniformity, which is critical for potent, low-dose compounds.

8.2 TYPES OF CAPSULES

Capsules are primarily classified into two main categories based on the nature and flexibility of their shell: Hard Gelatin Capsules and Soft Gelatin Capsules. Additionally, there is a growing third category of Non-Gelatin Alternatives designed to meet specific dietary or technical needs (Figure 8.1).

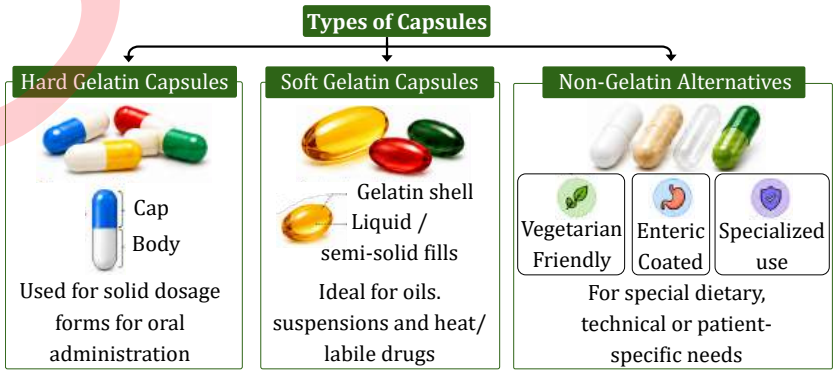


Figure 8.1: Classification of Capsules

The production of hard gelatin capsules occurs in two entirely separate phases: the manufacturing of the empty capsule shells and the subsequent filling of those shells with the active formulation.

A. Shell Manufacturing (Dip-Molding Process)

Empty hard capsule shells are manufactured on large, automated machines in strictly climate-controlled environments. The process involves the following sequential steps:

1. **Dipping:** Pairs of stainless steel mold pins (maintained at room temperature, around 22°C) are dipped into a heated, jacketed pan containing the gelatin solution (maintained between 45°C and 55°C).
2. **Spinning:** As the pins are slowly withdrawn from the solution, they are rotated to ensure the gelatin film distributes evenly over the mold.
3. **Drying:** The gelatin film sets and is then passed through a series of drying kilns where blasts of cool, controlled-humidity air remove the excess moisture.
4. **Stripping:** Bronze jaws grip the dried gelatin films and strip the cap and body portions off the mold pins.
5. **Trimming:** Stationary knives trim the stripped cap and body portions to their precise, required lengths (with a tolerance of ±0.15 mm).
6. **Joining:** The trimmed caps and bodies are mechanically joined together to a "prelock" position, allowing them to be transported without separating prior to the filling stage.

B. Capsule Filling Methods

Filling machines are primarily categorized by how they measure the dose of the powder.

1. **Dependent Filling (Auger Method):** This system uses the capsule body itself to measure the powder. The empty bodies pass under a hopper, and a revolving auger (screw) forces the powder into them. Uniformity relies entirely on completely filling the capsule body, meaning the dose is dependent on the capsule's volume and the powder's tapped bulk density.
2. **Independent Filling (Plug-Forming Methods):** Most industrial machines measure the powder independently of the capsule shell by compressing it into a soft compact, or "plug," using low compression force (10 to 100 N).
   - **Dosator System:** A dosing tube with a movable piston is lowered into the powder bed. The powder enters the tube, and the piston compresses it into a plug. The tube then moves over the empty capsule body, and the piston pushes the plug out.
   - **Tamping Finger and Dosing Disc:** A rotating disc contains precise cavities. As the disc rotates, sets of tamping fingers repeatedly press powder into the cavities to build up a plug in stages. At the final station, the plug is ejected into the capsule body.
3. **Bench-Scale Filling:** For small batches (50 to 10,000 capsules), manual devices (e.g., Feton plates) are used. Empty capsules are loaded into predrilled plastic plates, the caps are removed, and powder is spread manually over the bodies using a spatula.
   - **Alternative Fills (Pellets, Tablets, Liquids):** Modified dosing chambers or suction devices are used to fill granules and pellets. Liquid fills can be dosed using volumetric pumps; however, non-aqueous liquids require the two capsule halves to be hermetically sealed (e.g., via gelatin banding) to prevent leakage.

C. Finishing

Once filled, capsules undergo final finishing processes:

Polishing/Dusting: Capsules are cleaned to remove excess powder from the exterior. This is done using a coating pan (pan polishing), rubbing with an oil-impregnated cloth (cloth dusting), or passing them under rotating soft brushes with vacuum assistance.

Imprinting: Company logos or product identification markings are printed onto the shells.

II. Preparation of Soft Gelatin Capsules (SGC)

Unlike hard capsules, the formation, filling, and hermetic sealing of soft gelatin capsules occur simultaneously in a single, continuous operation (Figure 8.4)

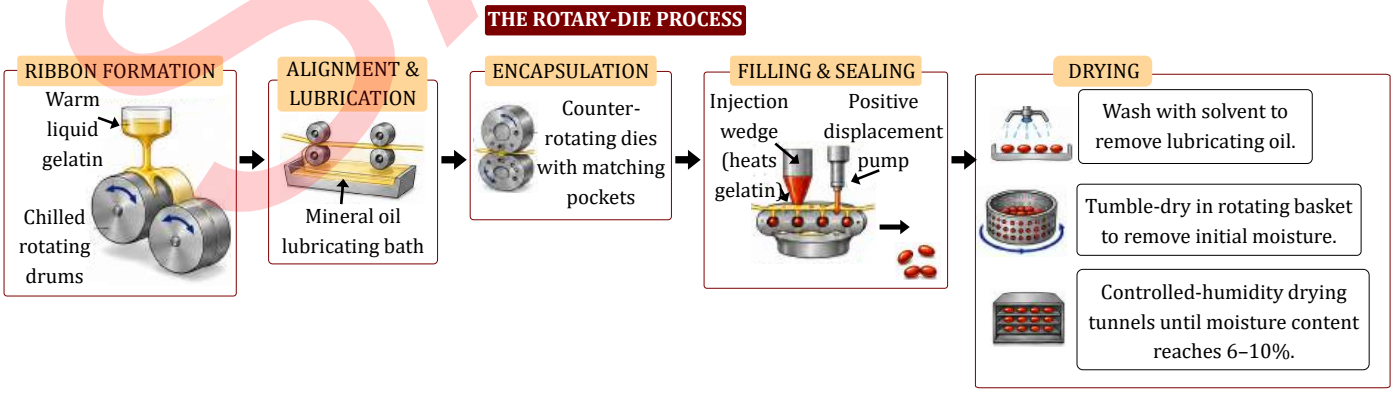


Figure 8.4: Preparation of Soft Gelatin Capsules (SGC)

9 MONOPHASIC LIQUID DOSAGE FORM

- **For internal use** – aromatic waters, syrups, elixirs and linctus (definition and preparation).
- **For external use and body cavities** – liniments, lotions, throat paints, applications, gargles, mouthwashes, enemas, eye drops, ear drops, nasal drops and tinctures with examples.
- **Study of official preparations-** Introduction to excipients and methods of preparation.

9.1 INTRODUCTION

Monophasic liquid dosage forms are pharmaceutical preparations consisting of a single, physically homogeneous phase. In these preparations, the drug or solute is completely and uniformly dissolved in a suitable liquid called the solvent or vehicle, which may be aqueous or non-aqueous. As the drug is distributed at the ionic or molecular level, the solute and solvent cannot be visually or physically distinguished, and every portion of the preparation contains a uniform dose. Monophasic liquids are relatively easy to prepare, administer and swallow, making them particularly useful for paediatric, geriatric and psychiatric patients who have difficulty taking solid dosage forms. They also allow flexible dose adjustment and generally provide faster drug absorption because the drug is already present in dissolved form. These preparations may be intended for internal, external or parenteral administration. Common examples include syrups, elixirs, linctuses, oral drops, draughts, gargles, mouthwashes, lotions, liniments, eye drops, ear drops, nasal drops, sprays and injections.

Table 9.1: Liquid Dosage Forms

Liquid Dosage Form	Definition	Primary Uses	Marketed Preparation (Examples)
Solution	A homogeneous liquid preparation in which one or more substances are completely dissolved in a suitable solvent or mixture of mutually miscible solvents.	Rapid drug absorption, oral and topical administration, pediatric and geriatric use.	Crocin® Oral Solution (Paracetamol), Benadryl® Cough Syrup
Syrup	A concentrated aqueous solution of sucrose or other sugars containing medicinal substances, flavoring agents, or both.	Oral administration, masking unpleasant taste, pediatric formulations.	Benadryl® Syrup, Ambrodil® Syrup, Ascoril® Syrup
Elixir	A clear, sweetened, flavored hydroalcoholic oral solution containing one or more active pharmaceutical ingredients.	Solubilization of drugs poorly soluble in water, oral administration.	Dexorange® Elixir, Liv-52® Elixir
Linctus	A viscous oral liquid preparation intended to be sipped slowly and swallowed without dilution for prolonged contact with the throat.	Relief of cough and sore throat.	Benadryl® Cough Linctus, Corex® Linctus
Oral Drops	Concentrated oral liquid preparations intended to be administered in small measured volumes using a calibrated dropper.	Pediatric dosing, vitamin supplementation, potent drugs.	D3 Must® Drops, Zincovit® Drops
Suspension	A biphasic liquid preparation containing finely divided insoluble solid particles dispersed uniformly in a liquid vehicle.	Administration of poorly soluble drugs, improved stability, taste masking.	Augmentin® Dry Syrup, Gelusil® Suspension, Digene® Suspension

2. **Solution by Agitation (Cold Process):** Utilized for heat-labile APIs or highly volatile flavors. Sucrose and medicinal ingredients are dissolved in purified water within a stainless steel or glass vessel utilizing continuous, prolonged mechanical agitation without any heat application.
3. **Addition of Sucrose to a Liquid Medication:** Often used when medicating a syrup with tinctures or fluid extracts. The concentrated liquid medication is added to an existing simple syrup. Care must be taken, as the dilution can cause alcohol-soluble resins in the tincture to precipitate.
4. **Percolation:** A cold extraction process. Purified water (or an aqueous solution of the drug) is allowed to slowly trickle down through a deep bed of crystalline sucrose packed inside a cylindrical percolator. As the fluid descends, it dissolves the sucrose, emerging at the bottom as a fully saturated syrup. Highly useful for botanical syrups like Ipecac syrup.

Cough and Cold Syrup

Cough and cold syrup is a combined oral liquid preparation used to relieve cough, nasal congestion and other symptoms associated with the common cold. Dextromethorphan hydrobromide acts as a cough suppressant, guaifenesin as an expectorant, chlorpheniramine maleate as an antihistamine and phenylephrine hydrochloride as a nasal decongestant. The remaining ingredients improve sweetness, viscosity, flavour, stability and preservation.

Table 9.7: Formulation of Cough and Cold Syrup

Ingredient	Quantity
Dextromethorphan hydrobromide	2.0 g
Guaifenesin	10.0 g
Chlorpheniramine maleate	0.2 g
Phenylephrine hydrochloride	1.0 g
Sodium benzoate	1.0 g
Saccharin sodium	1.9 g
Citric acid	1.0 g
Sodium chloride	5.2 g
Alcohol	50.0 mL
Sorbitol solution	324.0 mL
Syrup	132.0 mL
Liquid glucose	44.0 mL
Glycerin	50.0 mL
Colour	q.s.
Flavour	q.s.
Purified water, to make	1,000.0 mL

9.3.3 Elixirs

Elixirs are clear, pleasantly flavored, sweetened hydroalcoholic liquid preparations designed for oral administration. The major difference between a syrup and an elixir is the presence of ethanol as an essential component, which is usually present in a concentration range of 5% to 40% and acts as a primary co-solvent. Ethanol improves the solubility of many poorly water-soluble and lipophilic drugs, making elixirs highly effective vehicles for such medications. Formulations containing more than 20% alcohol possess inherent self-preserving properties due to the antimicrobial effect of ethanol.

Types of Elixirs

1. Non-Medicated Elixirs

Non-medicated elixirs do not contain any active therapeutic drug. They are mainly used as flavoured vehicles or diluting agents in the preparation of medicated elixirs. Common examples include Aromatic Elixir, Compound Benzaldehyde Elixir and Iso-alcoholic Elixir.

2. Medicated Elixirs

Medicated elixirs contain one or more active drugs and are used for therapeutic purposes. These include antihistamine elixirs for allergic symptoms, such as Diphenhydramine Elixir; sedative and hypnotic elixirs for producing sedation or sleep, such as Phenobarbital Elixir; bronchodilator elixirs for relieving bronchospasm, such as Theophylline Elixir; cardiac elixirs for certain heart conditions, such as Digoxin Elixir; and corticosteroid elixirs for controlling inflammation and allergic reactions, such as Dexamethasone Elixir.

Table 9.8: Examples of Elixers

Examples	Uses and Remarks
Adrenocortical Steroid	Used in rheumatoid arthritis, allergies, skin diseases and inflammatory conditions. Suitable for children and adults who have difficulty swallowing tablets.
Analgesic and Antipyretic	Used to relieve pain and reduce fever, particularly in patients who are sensitive to or unable to take aspirin.
Anticholinergic and Antispasmodic	Used to control gastric secretion, visceral spasms, gastrointestinal hypermotility and abdominal cramps.
Antihistamine	Used in allergic rhinitis, urticaria, allergic skin reactions and reactions to insect bites.
Antipsychotic	Used in the management of psychotic disorders.
Cardiotonic	Increases the force of myocardial contraction and is used in congestive heart failure, atrial fibrillation and other cardiac conditions.
Sedative and Hypnotic	Produces sedation at lower doses and hypnosis at higher doses.

10 SUSPENSIONS

- Definition and types (flocculated and deflocculated), advantages and disadvantages, formulation excipients and general methods of preparation.

10.1 INTRODUCTION

A pharmaceutical suspension is a specific type of biphasic, heterogeneous dispersed system. In this system, a finely divided, insoluble solid active ingredient is dispersed uniformly throughout a liquid dispersion medium. The internal phase consists of these insoluble solid particles, typically ranging in size from 0.5 to 5 micrometers. The external phase is generally aqueous, though it may sometimes be organic or an oil.

These dosage forms are versatile and can be administered orally, injected intramuscularly or subcutaneously, instilled intranasally, inhaled into the lungs, applied topically to the skin, or used for ophthalmic and otic purposes. According to the USP, preparations that require reconstitution prior to use are titled "for Oral Suspension," whereas prepared suspensions that do not require this step are simply designated as "Oral Suspension".

10.1.1 Ideal Characteristics

- The dispersed particles should not sediment rapidly.
- If a sediment does form, it must not compact into a hard cake at the bottom of the container and must re-disperse easily with moderate shaking.
- The viscosity must be perfectly balanced; if it is too high, the product becomes sticky in the oral cavity and difficult to swallow, but if it is too low, it creates pouring problems.
- The preparation must be physically, chemically, and microbiologically stable.
- It should have a pleasant odor, color, and palatability.
- Parenteral and ophthalmic suspensions require strict sterility and isotonicity, with ophthalmic suspensions restricted to a maximum particle size of 10 micrometers.
- Injectable forms must possess good syringe-ability.

10.2 PHYSICAL THERMODYNAMICS AND ELECTROKINETIC PRINCIPLES

Dispersed systems are heterogeneous systems in which an internal phase is distributed throughout a continuous external phase. Liquid-in-liquid dispersions form emulsions, whereas solid-in-liquid dispersions form suspensions. Based on particle size, they are classified as Amacroemulsions (0.1–10 μm), nanoemulsions (20–100 nm), thermodynamically stable microemulsions (5–50 nm) and multiple emulsions such as W/O/W. Macroemulsions and coarse suspensions are thermodynamically unstable because dispersion increases the interfacial area and free energy, expressed as $\Delta G_{form} = \gamma \Delta A - T\Delta S_{comf}$. This positive free energy promotes aggregation, coalescence and phase separation. Therefore, surfactants, polymers and finely divided solids are used to provide kinetic stability by modifying interfacial and electrokinetic forces. Their stabilizing effects are explained by the electrical double layer, DLVO theory and theories of emulsification.

10.2.1 The Electrical Double Layer

When a solid particle or liquid droplet is immersed in a polar liquid medium, it typically acquires a net surface charge. This charge may originate from the ionization of specific surface functional groups, the preferential adsorption of distinct ionic species from the bulk phase, or the oriented adsorption of dipolar molecules at the interface. Because the dispersed system must maintain overall macroscopic electroneutrality, the charged surface exerts an electrostatic pull on oppositely charged ions (counter-ions) in the surrounding medium while repelling ions of the same charge (co-ions). This specific, stratified arrangement of charges at the solid-liquid or liquid-liquid boundary is defined as the Electrical Double Layer (EDL). Over the past century, theoretical models describing the structure and potential distribution within the EDL have evolved sequentially, providing the mathematical foundation for modern colloid science (Figure 10.1).

10.2.2 The Helmholtz Parallel-Plate Model

The earliest theoretical framework for the EDL was postulated by Hermann von Helmholtz in 1853. Helmholtz

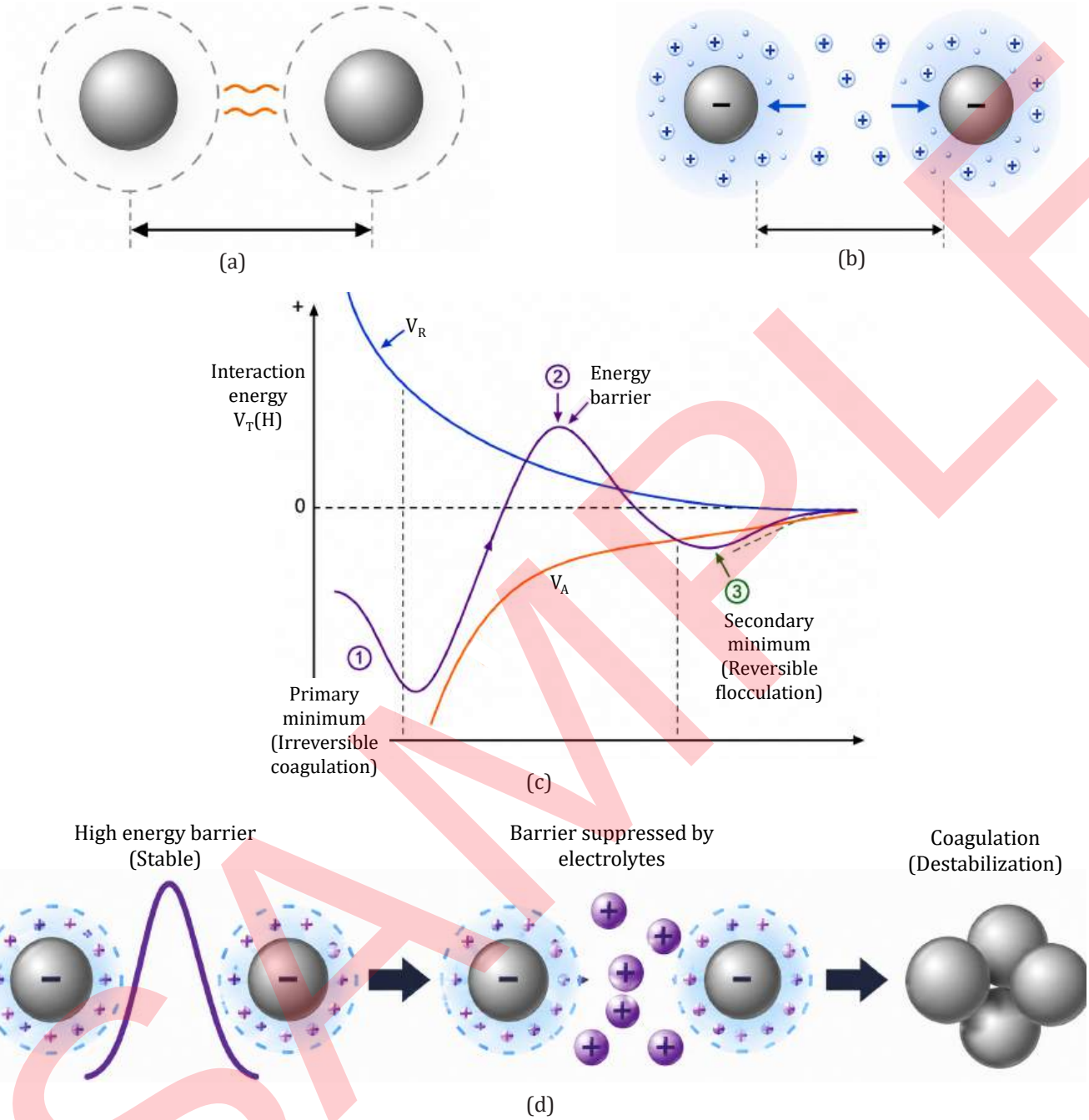


Figure 10.5: DLVO Theory: (a) Van Der Waals Attraction (Va); (b) Electrostatic Repulsion; (c) Dlvo Interaction Energy Profile; (d) Coagulation Kinetics

10.2.7 Dynamics and Stabilization of Suspensions

Solid-in-liquid suspensions present a unique stability challenge. Unlike emulsions, the internal solid phase does not coalesce; however, the particles are typically much denser than the continuous medium, rendering them highly susceptible to continuous, gravitationally driven sedimentation. The formulation paradigm centers entirely on manipulating particle-particle interactions to engineer the morphology of the resulting sediment. Suspensions are distinctly classified into two electrokinetic states: deflocculated and flocculated.

a. Sedimentation Parameters

To mathematically quantify the physical stability and terminal morphology of suspensions, two primary parameters are measured: the sedimentation volume (F) and the degree of flocculation (β).

b. Sedimentation Volume (F): Sedimentation volume is a macroscopic index used to describe the volume occupied by the settled phase of a suspension. It is defined as the ratio of the ultimate equilibrium volume of sediment (Vu) to the original total volume of suspension (Vo) before settling.

3. Incorporate into vehicle.
4. Mix thoroughly.
5. Make up final volume.

3. Paracetamol Suspension

Table 10.8: Formulation of Paracetamol Suspension

Ingredient	Quantity	Role
Paracetamol	2.4 g	API
Sodium CMC	0.75 g	Suspending agent
Tween 80	0.2 g	Wetting agent
Sucrose	40 g	Sweetener
Sodium Benzoate	0.1 g	Preservative
Flavor	q.s.	Palatability
Water	q.s.	Vehicle

Procedure

1. Wet paracetamol using Tween 80.
2. Prepare sodium CMC mucilage.
3. Add drug slowly into mucilage.
4. Dissolve sucrose separately.
5. Mix both portions.
6. Add preservative and flavor.
7. Make volume with water.

4. Chalk Mixture

Table 10.9: Formulation of Chalk Mixture (100 mL)

Ingredient	Quantity	Role
Prepared Chalk	10 g	Antacid
Tragacanth	0.5 g	Suspending agent
Syrup	20 mL	Sweetener
Chloroform Water	q.s.	Vehicle/preservative

Procedure

1. Triturate sulfur with glycerin.
2. Prepare bentonite dispersion.
3. Mix sulfur paste into dispersion.
4. Add remaining water gradually.
5. Mix until homogeneous.
6. Transfer to container.

General Labeling for Suspensions

- Shake well before use.
- Store in a tightly closed container.
- Do not freeze.
- Protect from excessive heat.

Reduce particle size (wetgrinding/levigation) → Add particles to the medium → Add wetting agent → Add structured vehicle / Add flocculating agent (OR) → Final suspension

(a)

Powder all solids and weigh. → Mix insoluble solid with some vehicle to make a smooth cream. → Add more vehicle to make the cream pourable. → Examine; if foreign particles, filter through muslin into tarred container. → Rinse mortar and pestle with vehicle & transfer washings to container. → Add any liquid ingredients (if any). → Make up final volume with vehicle and shake the bottle thoroughly.

(b)

Powder all solids and weigh. → Mix all ingredients & add compound tragacanth powder. → Measure 3/4 of the vehicle and triturate to a smooth cream. → Examine; filter through muslin into tarred bottle if particles visible. → Rinse mortar with vehicle and transfer to the bottle. → Add any liquid ingredients (if any). → Make up final volume, cork, label and dispense.

(c)

11 EMULSIONS

- Definition and types, emulsifying agents, tests for identification of types of emulsions, formulation excipients and general methods of preparation.

11.1 INTRODUCTION

An emulsion is a thermodynamically unstable, biphasic liquid dosage form made of two immiscible liquids usually oil and water. One liquid is uniformly dispersed as fine microscopic droplets (the internal or dispersed phase) throughout the other liquid (the external or continuous phase).

Because oil and water naturally repel each other due to differences in polarity, an emulsifying agent (or surfactant) is required. This agent works by reducing the interfacial tension between the two phases and forming a protective film around the droplets, preventing them from clumping back together.

Droplet sizes in standard pharmaceutical emulsions typically range from 0.1 to 100 µm, though specialized nanoemulsions can contain much smaller droplets (20 to 200 nm).

11.1.1 Need and Rationale for Emulsions

Formulating an emulsion goes far beyond simply mixing oil and water. It is a strategic approach to overcome severe physical and chemical limitations in drug delivery.

1. Solubilizing and Delivering Poorly Water-Soluble Drugs: Many modern active pharmaceutical ingredients (APIs) are highly lipophilic (fat-soluble) with terrible aqueous solubility. Dissolving lipophilic drugs (like Cyclosporine, Vitamin A, D, or E) into the internal oil phase allows them to be administered uniformly in a patient-friendly liquid form.

2. Dramatically Improving Oral Bioavailability: When lipophilic drugs are taken orally, they often suffer from poor gastrointestinal absorption. By presenting the drug dissolved in millions of microscopic oil droplets, an emulsion provides a massive surface area. This allows bile salts and pancreatic lipases to rapidly digest the lipids, speeding up absorption, promoting transport through the lymphatic system, and bypassing partial first-pass metabolism in the liver.

3. Masking Unpleasant Tastes and Odors: Therapeutic oils like castor oil, cod liver oil, or mineral oil taste and smell offensive. By formulating them as an O/W emulsion, the foul-tasting oil is "locked" inside the internal droplets, minimizing direct contact with the tongue's taste receptors. The external water phase can then be easily sweetened and flavored.

4. Protecting Sensitive Drugs from Degradation: Drugs that hydrolyze (degrade rapidly when exposed to water) or oxidize easily can be chemically shielded by dissolving them in the internal oil phase, extending their shelf life and stability.

5. Clinical and Nutritional Necessity: Pure oil cannot be injected into a vein it would cause a fatal embolism. However, sterile, ultra-fine O/W emulsions (like Intralipid®) allow hospitals to safely deliver essential lipids, fat-soluble vitamins, and high-calorie total parenteral nutrition (TPN) directly into a patient's bloodstream.

6. Controlled Release and Simultaneous Delivery: The oil droplets can act as tiny reservoirs, releasing a drug slowly over time for sustained-release depot injections. Furthermore, if a treatment requires both a water-soluble and an oil-soluble drug, an emulsion allows both to be delivered simultaneously in one dose.

11.1.2 Advantages

1. Pharmacokinetic and Therapeutic Optimization

- **Enhancement of Lipophilic Drug Bioavailability:** Many contemporary active pharmaceutical ingredients (APIs) exhibit suboptimal aqueous solubility, leading to poor dissolution and limited systemic absorption. Emulsions address this by solubilizing the lipophilic API within the dispersed internal phase. The microscopic droplet size yields a significantly expanded interfacial surface area, which facilitates rapid enzymatic degradation by gastrointestinal lipases and bile salts, thereby accelerating systemic absorption and promoting lymphatic transport while bypassing partial hepatic first-pass metabolism.

11.3.3 Oriented-Wedge Theory

Developed heavily by Harkins and Beeman in the 1920s, the Oriented-Wedge theory expands upon monomolecular adsorption by explicitly examining the geometrical architecture of the individual surfactant molecules. According to this model, amphiphiles can be viewed as wedges, with the shape dictated by the relative physical cross-sectional areas of their polar and non-polar domains.

When these "wedge-shaped" molecules pack tightly at an interface, they geometrically force the surface to adopt a specific curvature to achieve the most thermodynamically stable, void-free packing. If a surfactant possesses a massive polar headgroup and a narrow tail (e.g., highly hydrated monovalent soaps like sodium oleate), the optimal packing forces the interface to curve such that the narrow tails point inward, encapsulating the oil and yielding an O/W emulsion. Conversely, if the hydrophobic tail occupies a much larger volume than the headgroup (e.g., multivalent metallic soaps like calcium stearate), the interfacial film curves inversely to accommodate the bulky non-polar groups in the outer continuous phase, encapsulating water to yield a W/O emulsion. Thus, the macroscopic morphology of the emulsion is a direct manifestation of the microscopic geometry of the emulsifier.

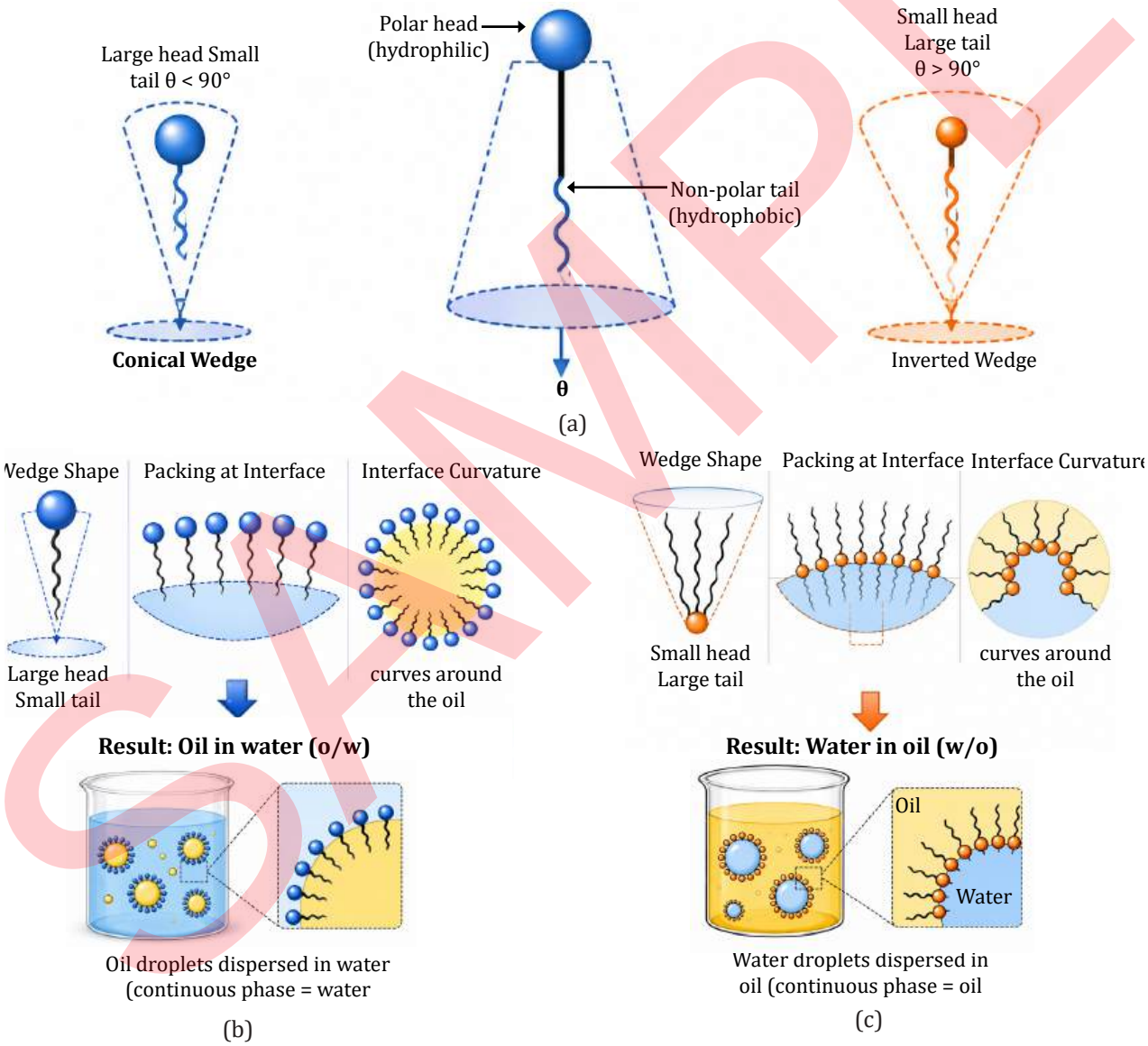


Figure 11.4: (a) Amphiphile as a Wedge; (b) Conical Wedge θ < 90°; (c)Inverted Wedge θ > 90°

11.3.4 Multimolecular Adsorption and the Plastic Film Theory

While synthetic surfactants stabilize primarily through interfacial tension reduction, macromolecular hydrophilic colloids such as natural gums (acacia, tragacanth), proteins (gelatin), and synthetic polymers operate via the Plastic or

11.8 STANDARD EMULSION PREPARATIONS

1. Liquid Paraffin Emulsion (Dry Gum Method; 4:2:1)

Table 11.5: Formulation of Liquid Paraffin Emulsion (100 mL)

Ingredient	Quantity	Role
Light Liquid Paraffin	40 mL	Oil phase (internal phase)
Acacia	10 g	Primary emulsifying agent
Purified Water	20 mL (for primary emulsion)	External phase
Purified Water	q.s. to 100 mL	Vehicle
Syrup	10 mL	Sweetening agent
Peppermint Water	10 mL	Flavoring agent

Procedure

1. Triturate acacia with liquid paraffin in a dry mortar.
2. Add water all at once.
3. Triturate rapidly until a creamy white primary emulsion forms.
4. Add syrup and peppermint water.
5. Transfer to a measuring cylinder.
6. Make up the volume with purified water.
7. Mix thoroughly and dispense.

2. Castor Oil Emulsion

Table 11.6: Formulation of Castor Oil Emulsion (100 mL)

Ingredient	Quantity	Role
Castor Oil	40 mL	Oil phase
Acacia	10 g	Emulsifying agent
Water	20 mL	Primary emulsion
Syrup	15 mL	Sweetener
Purified Water	q.s. to 100 mL	Vehicle

Procedure

1. Mix acacia with castor oil.
2. Add water rapidly.
3. Triturate until a stable primary emulsion develops.
4. Add syrup.
5. Adjust to volume with purified water.
6. Homogenize.

3. Cod Liver Oil Emulsion

Table 11.7: Formulation of Cod Liver Oil Emulsion (100 mL)

Ingredient	Quantity	Role
Cod Liver Oil	50 mL	Oil phase/API
Acacia	12.5 g	Emulsifier
Water	25 mL	Primary emulsion
Orange Syrup	10 mL	Flavor masking
Purified Water	q.s.	Vehicle

Procedure

1. Prepare primary emulsion using the dry gum method.
2. Incorporate orange syrup.
3. Make up volume with purified water.
4. Mix gently.

4. Mineral Oil Emulsion

Table 11.8: Formulation of Mineral Oil Emulsion (100 mL)

Ingredient	Quantity	Role
Mineral Oil	50 mL	Internal phase
Acacia	12.5 g	Emulsifying agent
Water	25 mL	Primary emulsion
Syrup	10 mL	Sweetener
Water	q.s.	Vehicle

Procedure

1. Triturate mineral oil with acacia.
2. Add water quickly.
3. Form primary emulsion.
4. Add syrup.
5. Dilute to final volume.

5. Olive Oil Emulsion

Table 11.9: Formulation of Olive Oil Emulsion (100 mL)

Ingredient	Quantity	Role
Ingredient	Quantity	Role
Olive Oil	40 mL	Oil phase
Acacia	10 g	Emulsifier
Water	20 mL	Primary emulsion
Purified Water	q.s.	Vehicle
Vanilla Flavor	0.2 mL	Flavor

Procedure

1. Mix olive oil and acacia thoroughly.

5. An emulsion freely diluted with water is:
(a) W/O emulsion (b) O/W emulsion
(c) O/W/O emulsion (d) Solid emulsion

6. Electrical conductivity is generally shown by:
(a) O/W emulsion (b) W/O emulsion
(c) Anhydrous oil (d) Oleaginous ointment

7. A blue-to-pink change in the cobalt chloride test indicates:
(a) W/O emulsion (b) O/W emulsion
(c) Cracked emulsion (d) Multiple emulsion

8. Which is a high-HLB non-ionic emulsifier?
(a) Span (b) Bentonite
(c) Polysorbate (d) Acacia

9. Sorbitan esters are commonly called:
(a) Tweens (b) Spans
(c) Carbomers (d) Parabens

10. Which agent forms a multimolecular film?
(a) Acacia
(b) Sodium lauryl sulphate
(c) Benzalkonium chloride
(d) Polysorbate 80

11. Hydrophilic particles with a contact angle below 90°90^\circ90° stabilize:
(a) W/O emulsion (b) O/W emulsion
(c) O/W/O emulsion (d) Aerosol

12. The fixed oil–water–gum ratio in the dry gum method is:
(a) 2:1:4 (b) 4:2:1
(c) 1:2:4 (d) 3:2:1

13. In the wet gum method, acacia is first mixed with:
(a) Oil (b) Alcohol
(c) Water (d) Preservative

14. The bottle method is suitable for:
(a) Viscous fixed oils (b) Volatile oils
(c) Semisolid waxes (d) Intravenous emulsions

15. In the beaker method, both phases are heated to:
(a) 20–25°C (b) 35–40°C
(c) 50–55°C (d) 70–75°C

16. Ultrasonication produces droplets mainly through:
(a) Filtration (b) Acoustic cavitation
(c) Sedimentation (d) Evaporation

17. Which instability is reversible by shaking?
(a) Cracking (b) Coalescence
(c) Creaming (d) Decomposition

18. Increasing continuous-phase viscosity:
(a) Increases creaming
(b) Decreases creaming
(c) Causes cracking
(d) Causes phase inversion

19. Which system is thermodynamically stable?
(a) Macroemulsion (b) Nanoemulsion
(c) Microemulsion (d) Coarse emulsion

20. SNEDDS form a fine emulsion in the presence of:
(a) Dry heat
(b) GI fluid and mild agitation
(c) High-pressure steam
(d) Organic solvent

ANSWER KEY

1-b	2-b	3-b	4-c	5-b	6-a	7-b	8-c	9-b	10-a
11-b	12-b	13-c	14-b	15-d	16-b	17-c	18-b	19-c	20-b

12 SEMISOLID DOSAGE FORMS

- Definitions, classification, advantages and disadvantages, ointment bases and other excipients used in semisolid dosage forms; general methods of preparation of ointments, pastes, creams and gels.

12.1 INTRODUCTION TO SEMISOLID DOSAGE FORMS

Semisolid dosage forms represent a foundational and highly diverse category of pharmaceutical preparations, strategically engineered to exist in a rheological state between solid and liquid matter. These viscoelastic systems are designed primarily for localized therapeutic action upon application to the skin or mucous membranes, though contemporary pharmacological advancements have firmly established their utility in systemic transdermal drug delivery. The formulation, manufacturing, and clinical deployment of these systems necessitate a profound understanding of physical chemistry, polymer science, cutaneous biology, and industrial engineering.

12.1.1 Physiological Fundamentals and Barrier Permeation

The rational design of a semisolid dosage form mandates an intricate understanding of the biological interfaces to which it is applied. The primary target for dermatological and transdermal formulations is the human skin, the largest organ of the body, comprising approximately ten percent of total body mass. The skin acts as a formidable, selectively permeable barrier designed to prevent desiccation, regulate thermodynamics, and protect the internal milieu against pathogenic, chemical, and ultraviolet insults.

Architecture of the Cutaneous Barrier

The human skin is histologically stratified into three distinct anatomical regions (Figure 12.1).

1. **The Epidermis:** The outermost, avascular layer of the skin, exhibiting significant regional variation in thickness, ranging from a delicate 0.06 mm on the eyelids to a robust 0.8 mm on the palmar and plantar surfaces. The most superficial sub-layer, the stratum corneum (often termed the 'horny layer'), is predominantly responsible for the barrier properties of human skin, actively limiting the permeation of chemical substances and microorganisms. When dry, the stratum corneum is 10 to 20 µm thick, though it possesses the capacity to swell to several times this dimension upon intense hydration. It consists of anucleated, flattened corneocytes densely packed with keratin filaments, enveloped within a highly organized lipid bilayer. This layer is composed of approximately 80% protein and 20% lipid, organized in a classic "brick and mortar" structural paradigm.
2. **The Dermis:** Positioned immediately beneath the epidermis, the dermis is a highly vascularized layer, 3 to 5 mm thick, composed of a complex connective tissue network of collagen and elastin fibers embedded within a mucopolysaccharide gel. This matrix provides an aqueous, hydrogel-like environment. Nerves, blood vessels, and lymphatics traverse this matrix, while skin appendages such as hair follicles, sebaceous glands, and sudoriferous (sweat) glands originate here and penetrate upward through the epidermis. If a drug molecule successfully traverses the stratum corneum and reaches the vascularized dermal layer, it becomes available for systemic absorption into the general circulation.
3. **The Subcutaneous Layer (Hypodermis):** The innermost layer, several millimeters thick, consists predominantly of adipose tissue. It provides mechanical cushioning, acts as a thermal barrier, and serves as an additional physiological reservoir for highly lipophilic drug molecules.

Mechanisms of Drug Permeation

Upon topical application, drug molecules partition from the semisolid vehicle into the stratum corneum and subsequently diffuse through the underlying tissues. The molecules navigate the intact stratum corneum via three recognized pathways:

- **Intercellular Route:** This represents the predominant pathway for the majority of drug molecules. Permeants must traverse the continuous, tortuous lipid domains existing between the corneocytes.
- **Intracellular (Transcellular) Route:** A polar pathway

Table 12.6 : Strong Iodine Ointment

Ingredient	Quantity (g)
Iodine	4
Potassium iodide	4
Wool fat	4
Yellow soft paraffin	76
Water	12
Upto	100

Potassium iodide is dissolved in water, followed by iodine. Wool fat and yellow soft paraffin are melted together and cooled to about 40°C. The iodine solution is added gradually with continuous stirring. The ointment is cooled and packed.

Ointment Containing Combined Iodine

Unsaturated vegetable and animal oils absorb iodine at their double bonds. This reaction forms iodinated compounds and produces a non-staining iodine preparation.

Table 12.7 : Non-Staining Iodine Ointment

Ingredient	Quantity
Iodine	5 g
Arachis oil	15 mL
Yellow soft paraffin	Sufficient quantity to produce 100 g
Upto	100 g

Iodine is mixed with arachis oil and heated at approximately 50°C until the colour changes to greenish-black. The iodized oil is then mixed with warmed yellow soft paraffin and packed in an amber-coloured container.

4. Preparation by Emulsification

The emulsification method is used for preparing creams and emulsion-type ointments. Such preparations contain an oil phase, an aqueous phase and an emulsifying agent.

For oil-in-water creams, emulsifying agents such as water-soluble soaps, cetyl alcohol, glyceryl monostearate and non-ionic surfactants may be used. Water-in-oil creams commonly contain beeswax and polyvalent ions such as calcium, magnesium or aluminium.

General Procedure

The oil-soluble ingredients, including fats, oils and waxes, are melted together at approximately 70°C. The aqueous phase containing water-soluble ingredients is separately heated to the same temperature. The aqueous phase is then added slowly to the oil phase with continuous stirring. Stirring is continued during cooling until a smooth, uniform and semisolid cream is formed.

Both phases should be maintained at approximately the same temperature to prevent premature solidification of waxes and fats.

12.5.2 Method of Preparation of Pastes

Pastes are stiff semisolid preparations intended for external application to the skin. They contain a high proportion of finely powdered medicaments, generally about 50%, dispersed in a suitable base. Due to their high solid content, pastes do not melt at ordinary temperatures and remain confined to the site of application.

Pastes form a thick protective layer over the affected area and absorb serous discharges from skin lesions. Therefore, they are commonly used as protective, antiseptic, absorbent and soothing dressings.

Table 12.8 : Differences Between Pastes and Ointments

Pastes	Ointments
Contain a high proportion of finely powdered solids (usually 20–50%).	Contain little or no finely powdered solids.
Thick, stiff, and less spreadable.	Soft, smooth, and easily spreadable.
Remain localized at the site of application.	Tend to spread to surrounding healthy skin.
Highly absorbent; absorb exudates and secretions.	Less absorbent and more occlusive.
Porous, allowing perspiration to escape.	Non-porous, may trap moisture.
Provide better protection to the skin.	Offer less protection against external irritants.
Less greasy.	More greasy and oily.
Less likely to cause skin maceration.	May cause greater skin maceration due to occlusive nature.
Suitable for oozing, inflamed, or weeping skin lesions.	Suitable for dry, scaly, or chronic skin conditions requiring emollient action.

Methods of Preparation

Pastes are mainly prepared by the following methods:

1. Trituration Method

The trituration method is used when the base is liquid or semisolid. The finely powdered ingredients are first sieved and mixed uniformly. They are then levigated with a small quantity of the base to form a smooth paste. The remaining base is incorporated gradually with continuous trituration until a homogeneous preparation is obtained.

2. Fusion Method

The fusion method is used when the paste contains solid or

13 SUPPOSITORIES & PESSARIES

- Definition, types of suppositories, advantages and disadvantages, formulation excipients used in suppositories, properties of ideal suppository bases, types of suppository bases, displacement value and general method of preparation.

13.1 INTRODUCTION

The development, formulation, and clinical application of suppositories and pessaries represent a highly specialized and enduring pillar of pharmaceutical science. By strict pharmacological definition, suppositories are solid dosage forms engineered for insertion into bodily orifices most prominently the rectum, vagina, or urethra where they undergo a precise state transition by melting, softening, or dissolving at physiological body temperatures to exert localized or systemic therapeutic effects.

The etymology of the term "suppository" provides immediate insight into its functional application; it is derived from the Latin root supponere, meaning "to place under," which itself is a linguistic amalgamation of the prefix sub (under) and the verb ponere (to place). This historical nomenclature elegantly mirrors the therapeutic mechanism of placing a medicinal compound under or into the body's lower cavities to achieve a desired medical outcome. The administration of medicinal and mechanical agents via bodily cavities possesses profound historical roots that predate modern allopathic medicine by millennia.

Suppositories are solid medicated dosage forms intended for insertion into body cavities such as the rectum, vagina, or urethra. After insertion, they melt, soften, or dissolve at body temperature and release the drug to produce either a local or systemic therapeutic effect.

The Rectal Environment

The terminal segment of the large intestine, measuring approximately 15 to 20 centimeters in length. It is generally not motile and lacks villi or microvilli entirely.

When devoid of fecal material, it contains only 2 to 3 milliliters of inert, highly viscous mucous fluid. This fluid scarcity poses a challenge for drug dissolution.

The submucosal region is densely vascularized. Drugs absorbed in the lower rectum are collected by the lower and middle hemorrhoidal veins, draining directly into the inferior vena cava. This completely bypasses the portal vein and hepatic first-pass metabolism, significantly increasing bioavailability for hepatically degraded drugs.

Rectal fluids maintain a neutral pH (7.0 to 7.4) and lack buffering capacity. Drugs remain in the chemical form in which they are administered.

Absorption is maximized in an empty rectum (often achieved via an evacuant enema). Diarrhea, colonic obstruction, and tissue dehydration negatively impact drug absorption.

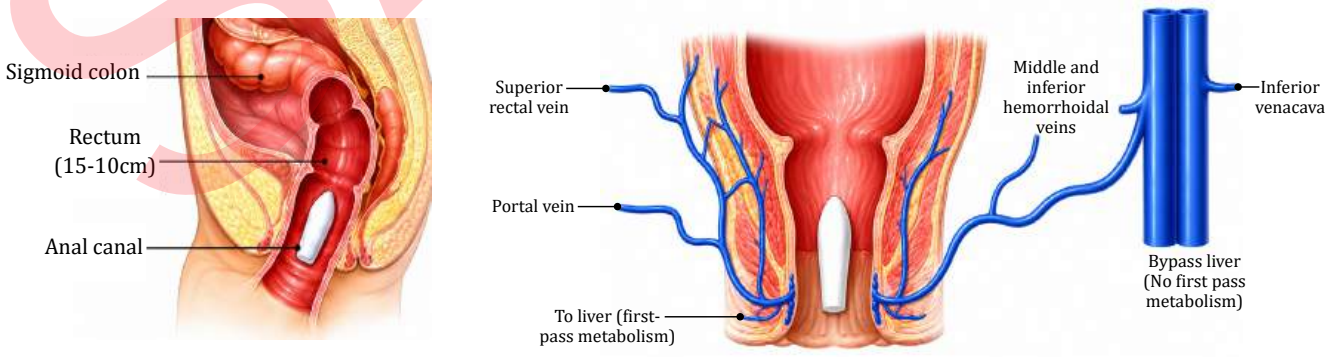


Figure 13.1 : The Rectal Environment

Disadvantages

- Generally, more expensive than natural cocoa butter.
- Can become brittle if cooled too rapidly during the manufacturing process.

Table 13.2: Classification and Characteristics of Witepsol Grades

Witepsol Grade	Distinguishing Chemical Property	Physical Effect
H15	Low hydroxyl value, <1% monoglycerides	Low viscosity, ideal for rapid molding
W35	High hydroxyl value, high diglycerides	Higher viscosity, enhanced aqueous emulsification
S55	Contains specialized additives (e.g., beeswax)	Altered melting point and solidification profile

13.5.2 Water-Soluble and Water-Miscible Bases

These bases do not melt; they slowly and steadily dissolve directly into mucosal fluids.

A. Polyethylene Glycols (PEGs / Macrogols): Synthetic polymers of ethylene oxide and water, distinguished by their molecular weight (e.g., PEG 300 to 8000). Formulations typically blend multiple PEG weights.

Advantages

- Can be engineered with melting points well above body temperature, permitting safe, indefinite storage at high ambient room temperatures without refrigeration.
- Does not melt and leak from the body cavity, improving patient comfort.
- Provides excellent, reliable release of hydrophobic (fat-soluble) drugs.

Disadvantages

- Highly hygroscopic; formulations with less than 20% internal water aggressively extract mucosal moisture upon insertion, triggering sharp stinging and local tissue irritation.
- Mandates patient counseling to pre-dip the suppository in water before insertion to mitigate stinging.

Table 13.3: Average Melting Ranges of Different Polyethylene Glycol (PEG) Grades

Polyethylene Glycol (PEG) Grade	Average Melting Range (°C)
PEG 300	-15 to -18
PEG 400	4 to 8
PEG 600	20 to 25
PEG 1000	37 to 40
PEG 1450	43 to 46
PEG 3350	54 to 58
PEG 4600	57 to 61
PEG 6000	56 to 63
PEG 8000	60 to 63

B. Glycerinated Gelatin: Typically compounded from 20% granular gelatin, 70% glycerin, and 10% water/API.

Advantages

- Slower to soften and dissolve, providing highly controlled, prolonged, and sustained local release (ideal for vaginal anti-infectives).

Disadvantages

- Profoundly hygroscopic; requires tight packaging to protect from atmospheric moisture and requires pre-moistening by the patient to prevent severe mucosal dehydration.
- The nutrient-rich gelatin matrix strongly supports microbial/fungal proliferation, necessitating the mandatory addition of chemical preservatives.

13.5.3 Miscellaneous and Emulsion Bases

Complex physical mixtures of lipophilic and hydrophilic compounds designed to hold large volumes of aqueous solutions. For example, Polyoxyl 40 stearate (a surface-active agent).

- **Advantages:** Facilitates rapid self-emulsification and enhanced spreading of the matrix upon contact with cavity fluids.
- **Disadvantages:** Can be structurally complex to formulate and may interact poorly with specific active ingredients.

13.6 DISPLACEMENT VALUE AND GENERAL METHOD OF PREPARATION.

13.6.1 The Displacement Value (DV)

Defined as the exact quantity (in grams) of a drug that displaces exactly 1 gram of the designated suppository base. (e.g., The DV of zinc oxide is 4.7, meaning 4.7 g of ZnO occupies the same physical volume as 1.0 g of cocoa butter).

Table 13.4: Displacement Values and Dosage Replacement Factors of Common Drugs in Cocoa Butter Base

Common Active Pharmaceutical Ingredient	Displacement Value (in Cocoa Butter)	Dosage Replacement Factor (f)
Zinc Oxide	4.0 - 4.7	0.15 - 0.25
Bismuth Subgallate	2.7	0.37

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