# UNIT – 1 **INTERPORT OF THE PROPERTY OF THE PRO**

# POINTS TO BE COVERED IN THIS TOPIC

- PARTIAL FRACTIONS
- ► LOGARITHMS iii
- ► FUNCTIONS @
- ► LIMITS AND CONTINUITY ∞

# PARTIAL FRACTIONS

# **► INTRODUCTION**

Partial fractions represent a fundamental algebraic technique used extensively in pharmaceutical mathematics, chemical kinetics, and pharmacokinetic calculations. This method involves decomposing complex rational fractions into simpler component fractions that are easier to integrate, differentiate, or manipulate algebraically.

The technique of partial fractions is particularly valuable in pharmacy practice for solving differential equations that arise in drug concentration calculations, reaction rate analysis, and compartmental modeling of drug distribution in biological systems.

#### **➤ POLYNOMIAL**

A polynomial is a mathematical expression consisting of variables and coefficients, involving operations of addition, subtraction, multiplication,

and non-negative integer exponents of variables.

**General Form:** 
$$P(x) = a_n x^n + a_{n-1} x^{n-1} + a_{n-2} x^{n-2} + ... + a_2 x^2 + a_1 x + a_0$$

Where:

- $a_n$ ,  $a_{n-1}$ , ...,  $a_1$ ,  $a_0$  are constants (coefficients)
- n is a non-negative integer (degree of polynomial)
- $a_n \neq 0$  (leading coefficient)

## **Classification by Degree:**

- Constant Polynomial (Degree 0): P(x) = a<sub>0</sub>
- **Linear Polynomial** (Degree 1):  $P(x) = a_1x + a_0$
- Quadratic Polynomial (Degree 2):  $P(x) = a_2x^2 + a_1x + a_0$
- Cubic Polynomial (Degree 3):  $P(x) = a_3x^3 + a_2x^2 + a_1x + a_0$

#### > RATIONAL FRACTIONS

A rational fraction is defined as the quotient of two polynomials, where the denominator polynomial is not zero.

**Mathematical Form:** R(x) = P(x)/Q(x)

Where:

- P(x) and Q(x) are polynomials
- $Q(x) \neq 0$
- P(x) is called the numerator polynomial
- Q(x) is called the denominator polynomial

# **Properties of Rational Fractions:**

- The domain excludes values that make Q(x) = 0
- Can be simplified by canceling common factors
- May have vertical asymptotes where Q(x) = 0
- Degree relationship determines behavior at infinity

#### ➤ PROPER AND IMPROPER FRACTIONS

## PROPER FRACTIONS

A rational fraction P(x)/Q(x) is called proper when the degree of the numerator polynomial P(x) is less than the degree of the denominator polynomial Q(x).

#### **Characteristics:**

- Degree of P(x) < Degree of Q(x)</li>
- The fraction approaches zero as x approaches infinity
- Always converges to a finite limit
- Can be directly decomposed into partial fractions

#### IMPROPER FRACTIONS A

A rational fraction P(x)/Q(x) is called improper when the degree of the numerator polynomial P(x) is greater than or equal to the degree of the denominator polynomial Q(x).

# **Characteristics:**

• Degree of  $P(x) \ge Degree of Q(x)$ 

- Must be converted to proper form before partial fraction decomposition
- Involves polynomial long division
- Results in quotient polynomial plus proper fraction remainder

#### > PARTIAL FRACTION DECOMPOSITION

Partial fraction decomposition is the process of expressing a single rational fraction as a sum of simpler fractions with linear or irreducible quadratic denominators.

Denominator Type	Partial Fraction Form	Number of Terms
Linear factors: (x-a) <sup>n</sup>	$A_1/(x-a) + A_2/(x-a)^2 + + A_n/(x-a)^n$	n terms
Quadratic factors: (ax²+bx+c) <sup>m</sup>	$(A_1x+B_1)/(ax^2+bx+c) + + (A_mx+B_m)/(ax^2+bx+c)^m$	m terms
Mixed factors	Combination of above forms	Variable <b>•</b>

### ➤ RESOLVING INTO PARTIAL FRACTIONS

The systematic approach to resolve rational fractions into partial fractions involves several distinct cases:

#### **CASE 1: Distinct Linear Factors**

For denominator  $Q(x) = (x-a_1)(x-a_2)...(x-a_n)$  where all factors are different:

$$P(x)/Q(x) = A_1/(x-a_1) + A_2/(x-a_2) + ... + A_n/(x-a_n)$$

## Method to find constants:

- Cover-up Method: Multiply both sides by  $(x-a_i)$  and substitute  $x = a_i$
- Comparison of Coefficients: Expand and equate coefficients
- **Substitution Method**: Use convenient values of x

## **CASE 2: Repeated Linear Factors**

For denominator containing factor (x-a)<sup>m</sup>:

$$P(x)/((x-a)^mQ_1(x)) = A_1/(x-a) + A_2/(x-a)^2 + ... + A_m/(x-a)^m + [terms from Q_1(x)]$$

## **CASE 3: Irreducible Quadratic Factors**

For denominator containing factor ( $ax^2+bx+c$ ) where  $b^2-4ac < 0$ :

$$P(x)/((ax^2+bx+c)Q_1(x)) = (Ax+B)/(ax^2+bx+c) + [terms from Q_1(x)]$$

# ➤ APPLICATION IN CHEMICAL KINETICS AND PHARMACOKINETICS

# Chemical Kinetics Applications

**First-Order Reactions:** In first-order kinetic processes, the rate equation leads to:  $\int 1/(a-x) dx = -\ln(a-x)/k + C$ 

**Second-Order Reactions:** For reactions of type A + B  $\rightarrow$  Products:  $\int 1/((a-x)(b-x)) dx$  requires partial fraction decomposition

**Competitive Inhibition:** Enzyme kinetics with competitive inhibition involves rational fractions in Lineweaver-Burk plots.

# Pharmacokinetic Applications 🥕

**One-Compartment Model:** Drug elimination following first-order kinetics:  $C(t) = C_0 e^{-(-kt)}$ 

**Two-Compartment Model:** Distribution and elimination involve biexponential decay:  $C(t) = Ae^{-\alpha t} + Be^{-\alpha t}$ 

**Clearance Calculations:** Total body clearance relationships often require partial fraction analysis for complex elimination pathways.

Kinetic Model	<b>Equation Type</b>	Partial Fraction Application
First-order elimination	Exponential decay	Direct integration
Michaelis-Menten	Rational function	Lineweaver-Burk linearization
Two-compartment Biexponential Residual method analysis		Residual method analysis
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# **II** LOGARITHMS

## **➤ INTRODUCTION**

Logarithms represent one of the most powerful mathematical tools in pharmaceutical sciences, providing essential methods for handling exponential relationships, pH calculations, drug potency measurements, and pharmacokinetic analysis. The logarithmic function serves as the inverse of exponential functions and appears frequently in biological and chemical processes.

In pharmacy practice, logarithms are indispensable for calculations involving pH and pKa values, drug concentration relationships, enzyme kinetics, and bioavailability studies. Understanding logarithms enables

pharmaceutical professionals to work effectively with exponential processes that characterize many biological systems.

## **➤ DEFINITION**

A logarithm is the exponent to which a base must be raised to produce a given number.

**Mathematical Definition:** If  $b^y = x$ , then  $log_b(x) = y$ 

### Where:

- **b** is the base (b > 0, b ≠ 1)
- $\mathbf{x}$  is the argument (x > 0)
- **y** is the logarithm
- log\_b(x) is read as "logarithm of x to base b"

## **Special Cases:**

- Common Logarithm:  $log_{10}(x) = log(x)$
- Natural Logarithm: log\_e(x) = ln(x)
- **Binary Logarithm**: log<sub>2</sub>(x)

# ➤ THEOREMS/PROPERTIES OF LOGARITHMS

## **FUNDAMENTAL PROPERTIES**

**Property 1: Product Rule**  $log_b(xy) = log_b(x) + log_b(y)$ 

Application: Used in pharmaceutical calculations when combining multiplicative factors.

**Property 2: Quotient Rule**  $log_b(x/y) = log_b(x) - log_b(y)$ 

Application: Essential for ratio calculations in drug concentration studies.

**Property 3: Power Rule**  $log_b(x^n) = n \cdot log_b(x)$ 

Application: Critical for handling exponential relationships in pharmacokinetics.

**Property 4: Base Change Formula**  $log_b(x) = log_a(x)/log_a(b) = ln(x)/ln(b)$ 

Application: Enables conversion between different logarithmic bases.

#### **ADDITIONAL PROPERTIES**

# **Property 5: Identity Properties**

- log\_b(b) = 1
- $\log_b(1) = 0$
- $log_b(b^x) = x$
- $b^{(\log_b(x))} = x$

**Property 6: Reciprocal Property**  $log_b(1/x) = -log_b(x)$ 

**Property 7: Root Property**  $\log_b(^n \sqrt{x}) = \log_b(x^{(1/n)}) = (1/n) \cdot \log_b(x)$ 

### > COMMON LOGARITHMS

Common logarithms use base 10 and are extensively employed in pharmaceutical calculations, particularly for pH measurements, drug potency determinations, and concentration calculations.

**Standard Form:**  $log_{10}(x) = log(x)$ 

# **Key Values:**

- log(1) = 0
- log(10) = 1
- log(100) = 2
- log(1000) = 3
- log(0.1) = -1
- log(0.01) = -2

# > CHARACTERISTIC AND MANTISSA

Every common logarithm can be expressed as the sum of two components: the characteristic and the mantissa.

# CHARACTERISTIC [[]

The characteristic is the integer part of the logarithm, indicating the power of 10.

# **Rules for Determining Characteristic:**

- For numbers ≥ 1: Characteristic = (number of digits before decimal) 1
- For numbers < 1: Characteristic = -(number of zeros immediately after decimal point)

#### **MANTISSA**

The mantissa is the positive decimal part of the logarithm, always between 0 and 1.

# **Properties of Mantissa:**

- Always positive regardless of the sign of characteristic
- Determined from logarithm tables or calculators
- Independent of the position of decimal point in the original number

Characteristic	Mantissa	Complete Logarithm
2	0.3702	2.3702
1	0.3702	1.3702
0	0.3702	0.3702
-1	0.3702	-1 + 0.3702 = -0.6298
-2	0.3702	-2 + 0.3702 = -1.6298
	2 1 0	2 0.3702 1 0.3702 0 0.3702 -1 0.3702

# ➤ APPLICATION OF LOGARITHMS IN PHARMACEUTICAL PROBLEMS

# pH and pOH Calculations

**Henderson-Hasselbalch Equation:**  $pH = pKa + log([A^-]/[HA])$ 

**Buffer Calculations:** pH = pKa + log(concentration of salt/concentration of acid)

**Ion Product of Water:**  $pH + pOH = 14 [H^{+}][OH^{-}] = 10^{-14}$ 

# Drug Potency and Bioassay 🎺

**Dose-Response Relationships:** log(dose) vs response plots for determining  $ED_{50}$ ,  $LD_{50}$ 

**Michaelis-Menten Kinetics:** Lineweaver-Burk plot: 1/V = (Km/Vmax)(1/[S]) + 1/Vmax

#### **Pharmacokinetic Parameters:**

• Half-life:  $t_1/_2 = 0.693/k$ 

Elimination rate constant: k = ln(2)/t<sub>1</sub>/<sub>2</sub>

#### Concentration and Dilution Calculations

**Beer-Lambert Law:** A =  $\epsilon bc = log(l_0/l)$ 

**Serial Dilutions:** log(final concentration) = log(initial concentration) + n·log(dilution factor)

# **©** FUNCTIONS

#### ➤ REAL VALUED FUNCTION

A real valued function is a mathematical relationship that assigns exactly one real number (output) to each element in its domain (input) from the set of real numbers.

**Formal Definition:** A function  $f: A \rightarrow B$  is called a real valued function if:

- $A \subseteq \mathbb{R}$  (domain is subset of real numbers)
- $B \subseteq \mathbb{R}$  (codomain is subset of real numbers)
- For each  $x \in A$ , there exists exactly one  $y \in B$  such that f(x) = y

# **Components of a Function:**

- **Domain**: Set of all possible input values (x-values)
- Codomain: Set of all possible output values
- Range: Set of actual output values
- **Rule of Assignment**: Mathematical expression defining the relationship

#### ➤ CLASSIFICATION OF REAL VALUED FUNCTIONS

#### BASED ON MATHEMATICAL FORM

Function Type	General Form	Pharmaceutical Application	
Linear	f(x) = mx + c	Drug dissolution kinetics	
Quadratic	$f(x) = ax^2 + bx + c$	Dose-response curves	
Exponential	$f(x) = a^{bx}$	Drug elimination	
Logarithmic	$f(x) = log_a(x)$	pH calculations	
Trigonometric	$f(x) = \sin(x), \cos(x)$	Biorhythms, oscillatory processes	
Rational	f(x) = P(x)/Q(x)	Michaelis-Menten kinetics	
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#### **BASED ON BEHAVIOR CHARACTERISTICS**

- **1. Continuous Functions** Functions without breaks, jumps, or holes in their graphs.
  - Drug concentration curves
  - Temperature variation functions
  - Smooth dose-response relationships

- **2. Discontinuous Functions** Functions with breaks or jumps at certain points.
  - Step-wise dosing regimens
  - On-off drug release mechanisms
  - Threshold response functions
- 3. Monotonic Functions Functions that consistently increase or decrease.
  - Increasing:  $f(x_1) < f(x_2)$  when  $x_1 < x_2$
  - **Decreasing**:  $f(x_1) > f(x_2)$  when  $x_1 < x_2$
- **4. Periodic Functions** Functions that repeat their values at regular intervals. f(x + T) = f(x) for all x, where T is the period.

#### **BASED ON DOMAIN-RANGE RELATIONSHIPS**

- **1. One-to-One Functions (Injective)** Each element in the range corresponds to exactly one element in the domain.
  - Horizontal line test: passes
  - Has an inverse function
  - Example: Drug clearance as function of body weight
- 2. Onto Functions (Surjective) Range equals the codomain.
  - Every possible output value is achieved
  - Complete utilization of target space
- **3. Bijective Functions** Functions that are both one-to-one and onto.

- Perfect correspondence between domain and range
- Invertible functions
- Example: Temperature conversion functions

#### **SPECIAL PHARMACEUTICAL FUNCTIONS**

- **1. Sigmoid Functions** S-shaped curves commonly seen in dose-response relationships:  $f(x) = 1/(1 + e^{-x})$
- **2. Michaelis-Menten Function** Describes enzyme kinetics:  $v = (V_max \times [S])/(K_m + [S])$
- **3. Exponential Decay Functions** Characterizes drug elimination:  $C(t) = C_0 \times e^{-kt}$
- **4. Hill Function** Models cooperative binding:  $f(x) = x^n/(K^n + x^n)$

#### **COMPOSITE FUNCTIONS**

**Definition:** If f: A  $\rightarrow$  B and g: B  $\rightarrow$  C, then the composite function gof: A  $\rightarrow$  C is defined by:  $(g \circ f)(x) = g(f(x))$ 

# **Properties:**

- Composition is associative: (hog)of = ho(gof)
- Generally not commutative: g∘f ≠ f∘g
- Identity function is neutral: fol = lof = f

## **Pharmaceutical Applications:**

- Sequential metabolic processes
- Multi-step drug delivery systems

• Cascade reactions in biochemical pathways

## INVERSE FUNCTIONS

**Definition:** If f: A  $\rightarrow$  B is bijective, then f<sup>-1</sup>: B  $\rightarrow$  A exists such that: f<sup>-1</sup>(f(x)) = x and f(f<sup>-1</sup>(y)) = y

# **Properties:**

- Domain of f<sup>-1</sup> = Range of f
- Range of f<sup>-1</sup> = Domain of f
- $(f^{-1})^{-1} = f$
- Graph of  $f^{-1}$  is reflection of f about y = x

# **Finding Inverse Functions:**

- 1. Replace f(x) with y
- 2. Interchange x and y
- 3. Solve for y
- 4. Replace y with  $f^{-1}(x)$

### **∞ LIMITS AND CONTINUITY**

#### **➤ INTRODUCTION**

Limits and continuity form the foundational concepts of calculus and are essential for understanding the behavior of pharmaceutical functions, particularly in pharmacokinetics, drug dissolution studies, and bioavailability analysis. These concepts help describe what happens to function values as input approaches specific points or infinity.

In pharmaceutical mathematics, limits are crucial for modeling steady-state conditions, analyzing rate processes, and understanding the behavior of drug concentration curves. Continuity ensures that small changes in dosing or timing produce predictable changes in therapeutic outcomes.

#### ➤ LIMIT OF A FUNCTION

The concept of limit describes the behavior of a function as its input approaches a particular value, without necessarily reaching that value.

**Intuitive Understanding:** A limit represents the value that a function approaches as the input gets arbitrarily close to a specific point, regardless of whether the function is actually defined at that point.

Notation:  $\lim[x \rightarrow a] f(x) = L$ 

Read as: "The limit of f(x) as x approaches a equals L"

#### **▶** DEFINITION OF LIMIT OF A FUNCTION

#### FORMAL $(\epsilon-\delta)$ DEFINITION $\wedge$

For a function f(x) and real numbers a and L:

$$\lim[x \to a] f(x) = L$$

if and only if for every  $\epsilon > 0$ , there exists  $\delta > 0$  such that: whenever  $0 < |x - a| < \delta$ , then  $|f(x) - L| < \epsilon$ 

#### **Components Explained:**

- ε (epsilon): Represents how close f(x) must be to L
- δ (delta): Represents how close x must be to a
- 0 < |x a|: Ensures x ≠ a (x approaches but doesn't equal a)
- $|f(x) L| < \varepsilon$ : f(x) stays within  $\varepsilon$ -neighborhood of L

#### **TYPES OF LIMITS**

- **1. Left-Hand Limit**  $\lim[x \to a^-]$   $f(x) = L_1$  (x approaches a from values less than a)
- **2. Right-Hand Limit**  $\lim[x \to a^{+}] f(x) = L_{2} (x \text{ approaches a from values greater than a)$
- **3. Two-Sided Limit**  $\lim[x \to a] f(x) = L$  exists if and only if:  $\lim[x \to a^-] f(x) = \lim[x \to a^+] f(x) = L$

## LIMIT THEOREMS AND PROPERTIES

Property	Formula	Condition	
Sum Rule	$\lim[x \to a] [f(x) + g(x)] = \lim[x \to a] f(x)$	Both limits exist	
	+ lim[x→a] g(x)		
Difference	$\lim[x \to a] [f(x) - g(x)] = \lim[x \to a] f(x)$	Both limits exist	
Rule	- lim[x→a] g(x)		
Product Rule	$\lim[x \to a] [f(x) \cdot g(x)] = \lim[x \to a] f(x) \cdot$	Both limits exist	
	lim[x→a] g(x)		
Quotient Rule	$\lim[x \to a] [f(x)/g(x)] = \lim[x \to a] f(x) /$	Both limits exist,	
	lim[x→a] g(x)	denominator ≠ 0	
Constant	limby all fof(y)] — alimby all f(y)	Limit oviete	
Multiple	$\lim[x \to a] [c \cdot f(x)] = c \cdot \lim[x \to a] f(x)$	Limit exists	
Power Rule	$\lim[x \to a] [f(x)]^n = [\lim[x \to a] f(x)]^n$	Limit exists	
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# **INDETERMINATE FORMS**

Situations where direct substitution leads to undefined expressions:

## **Common Indeterminate Forms:**

- 0/0
- ∞/∞
- 0.∞
- ∞ ∞
- 0°
- 1^∞
- $\bullet \quad \infty^0$

# **Resolution Techniques:**

- L'Hôpital's Rule: For 0/0 and ∞/∞ forms
- Algebraic Manipulation: Factoring, rationalization
- Trigonometric Identities: For trigonometric limits
- Standard Limits: Using known limit results

#### **➤ CONTINUITY**

#### **DEFINITION OF CONTINUITY**

A function f(x) is continuous at point x = a if:

- 1. f(a) exists (function is defined at a)
- 2.  $\lim_{x\to a} f(x)$  exists (limit exists at a)
- 3.  $\lim[x \to a] f(x) = f(a)$  (limit equals function value)

**Mathematical Notation:** f is continuous at  $a \Leftrightarrow \lim[x \to a] f(x) = f(a)$ 

#### **TYPES OF CONTINUITY**

- **1. Point Continuity** Continuity at a specific point as defined above.
- **2. Interval Continuity** A function is continuous on an interval if it's continuous at every point in that interval.
- **3. Uniform Continuity** A stronger form of continuity where the  $\delta$  in the continuity definition can be chosen independently of the point.

#### **TYPES OF DISCONTINUITIES**

1. Removable Discontinuity

- Function has a limit at the point
- Either function is undefined or limit ≠ function value
- Can be "fixed" by redefining the function at that point

# 2. Jump Discontinuity

- Left and right limits exist but are not equal
- Function "jumps" from one value to another
- Common in step-wise dosing protocols

# 3. Infinite Discontinuity

- Function approaches ±∞ as x approaches the point
- Vertical asymptotes
- Example: Drug concentration models with zero-order elimination

#### PHARMACEUTICAL APPLICATIONS OF LIMITS AND CONTINUITY

- **1. Steady-State Analysis**  $\lim_{t\to\infty} [t\to\infty] C(t) = C_ss$  (steady-state concentration)
- **2. Bioavailability Studies**  $\bowtie$   $\lim[t\to\infty]$  [AUC(0 $\to$ t)] = AUC(0 $\to\infty$ )
- **3. Enzyme Kinetics** =  $\lim[S \to \infty] v = V_{max}$  (maximum velocity)  $\lim[S \to 0] v = (V_{max}/K_m) \cdot [S]$  (first-order region)
- **4. Drug Release Kinetics** Continuity ensures smooth, predictable drug release profiles without sudden jumps or breaks.

Application	Function	Continuity	Clinical
Area	Туре	Requirement	Significance
Drug	Exponential	Continuous	Predictable
Concentration	decay	everywhere	therapeutic levels
Dose-Response	Sigmoid	Continuous on	Smooth therapeutic
	curves	domain	response
pH Titration	Logarithmic	Continuous except at	Accurate buffer
	Logarithmic	endpoints	calculations
Enzyme Kinetics	Rational	Continuous except at	Reliable kinetic
	functions	poles	parameters
4	•	•	

# IMPORTANT LIMIT RESULTS FOR PHARMACEUTICAL CALCULATIONS

#### **Standard Limits:**

- $\lim[x\to 0] (\sin x)/x = 1$
- $\lim[x\to 0] (1-\cos x)/x^2 = 1/2$
- $\lim[x\to\infty] (1 + 1/x)^x = e$
- $\lim[x\to 0] (e^x 1)/x = 1$
- $\lim[x\to 0] (\ln(1+x))/x = 1$

These fundamental concepts of limits and continuity provide the mathematical foundation necessary for advanced pharmaceutical calculations, ensuring precise and reliable therapeutic outcomes in clinical practice.