BT308

Tissue Engineering

Definition:

Tissue engineering is an interdisciplinary field that uses a combination of cells, engineering principles, and materials (often called scaffolds) to repair, replace, or enhance biological tissues.

Key Components:

- **Cells:**
  - **Stem Cells:** These can differentiate into various cell types (e.g., embryonic, adult, or induced pluripotent stem cells) and are used to form new tissues.
  - **Differentiated Cells:** Specialized cells taken from the body that can be encouraged to grow or repair tissue.
- **Scaffolds:**
  - These are 3D structures that support cell attachment, growth, and organization.
  - They can be made from natural materials (like collagen) or synthetic polymers.
  - The scaffold design must mimic the natural extracellular matrix of the tissue.
- **Growth Factors and Bioreactors:**
  - **Growth Factors:** Proteins or molecules that signal cells to proliferate or differentiate.
  - **Bioreactors:** Devices that provide a controlled environment (nutrients, oxygen, mechanical stimulation) to enhance tissue growth before implantation.

Scaffolds & Biomaterials

Scaffolds are needed because cells themselves cannot form structures and it can be inside or outside but only thing is it shouldn't be rejected by the body so it should be biocompatible.

Size, chemical-complexity, conformation genetics determine rejection of foreign substance.

Scaffold Properties:

- **Biocompatibility:**
  - Materials must be **Biodegradable (**The scaffold should gradually degrade as new tissue forms, ideally at a rate matching tissue regeneration**),** non-toxic, not elicit an immune response, and support cell function.
  - non-toxic may not be not elicit immunoresponse but can cause toxicity in some organs
  - Outside leaching can happen on contact
  - **Bone Density and Mechanical Stimulation**
    - **"Baby's bone density changes over time"**: Babies' bones grow and strengthen partly because of the mechanical forces they experience as they learn to crawl, stand, and walk.
    - Bones have **receptors** that sense load or stress (mechanical signals). When bones are regularly stressed in healthy ways, they respond by increasing density. This is why regular activity (dynamic environment) helps maintain or improve bone density.
  - **Muscle Gain in the Gym**
    - The same principle applies to **muscle tissue**: when you lift weights or exercise (another dynamic environment), your muscles sense the increased workload and adapt by growing in size and strength.
- **Blood Vessels in a Bioreactor**
  - In tissue engineering, if you want to grow blood vessels (or any tissue) in a lab setting, you often use a **bioreactor**.

    - A bioreactor can provide **constant flow**, nutrients, and the right mechanical cues (like pressure or shear stress for blood vessels). This "flow" environment mimics what happens inside the body, helping cells organize themselves into a functional vessel.

- **Scaffold Biodegradability**
    - When engineering new tissues (e.g., bone, cartilage, blood vessels), cells are often seeded onto a **scaffold**—a 3D structure that provides an initial shape and support.
    - This scaffold should ideally be **biodegradable** (for example, made from proteins or other materials that naturally break down).
    - As the cells grow and produce their own extracellular matrix, the scaffold gradually degrades, leaving behind the new, healthy tissue in the correct shape without permanent foreign materials.

- Adherent vs. Non-Adherent Cells
    - **Adherent cells**: These need to attach to a surface (like a flask or plate) to grow. Many mammalian cell types (e.g., fibroblasts, epithelial cells) are adherent.
    - **Non-adherent cells**: These grow in suspension (floating) and do not need to attach to a surface (e.g., many blood cells, immune cells).

- Stem Cells and Their Differentiation Potential
    - **Stem cells** have the ability to become many different kinds of cells. The notes mention several levels of "potency":
        1. **Totipotent**: Can become **any** cell type in the body **and** can form extra-embryonic tissues (like the placenta).
        2. **Pluripotent**: Can give rise to **any** cell type in the body (but **not** extra-embryonic tissues).
        3. **Multipotent**: Can differentiate into **several** related cell types (e.g., hematopoietic stem cells can become red blood cells, white blood cells, platelets, etc.).

4. **Unipotent**: Can produce **only one** specific cell type, but they still have self-renewal properties.

- **Embryonic stem cells** are typically **pluripotent** (they can become virtually any cell in the body). They are considered "best" for broad research applications because of their high potential, but they also raise ethical concerns and can carry a risk of forming teratomas (tumors) if not carefully controlled.

- Primary Cells vs. Cell Lines
  - **Primary cells**: These are directly taken from living tissue. They have more "realistic" characteristics (closer to the in vivo state) but usually do not proliferate indefinitely.
  - **Cell lines**: These are cells adapted to grow continuously in culture (often via some genetic modification or selection). They are typically:
    - **Less expensive** and easier to maintain in the long run.
    - **More stable** in terms of handling, but sometimes less physiologically "authentic" compared to primary cells.

- Autologous, Allogeneic, and Xenogenic Cells
  - **Autologous**: Cells or tissues derived from the same individual (e.g., using your own stem cells for therapy).
  - **Allogeneic**: Cells or tissues taken from a donor of the **same species** (e.g., a kidney transplant from another human).
  - **Xenogenic**: Cells or tissues derived from a **different species** (e.g., using pig valves in heart surgery).

Types of Biomaterials:

- **Polymers:**
  - Often biodegradable (e.g., polylactic acid, polyglycolic acid) and can be engineered to have specific mechanical properties.
- **Ceramics:**
  - Useful for hard tissues like bone due to their high compressive strength.

- **Metals:**
  - Metals like vandium, titanium or stainless steel are used where high strength is needed. They are often used in load-bearing implants.
- **Composites:**
  - Combining two or more materials to optimize performance (for example, combining polymers with ceramics to balance flexibility and strength).
- Metals in Implants
  - **Fe (Iron), Co (Cobalt), Ni (Nickel), Ti (Titanium), Ta (Tantalum)** are all metals commonly used (or alloyed) for biomedical implants.
  - These metals are often combined with other elements to form **alloys** that balance **strength, corrosion resistance, and biocompatibility**.

- Stainless Steel Basics
  - **"18-8 stainless steel"**: This typically refers to **304 stainless steel**, containing about **18% Chromium** and **8% Nickel**.
    - Chromium (Cr) helps form a protective **oxide layer** on the surface (which gives stainless steel its "stainless" property).
    - Nickel (Ni) helps with **corrosion resistance** and **mechanical properties**.
    - **Carbon content** in standard 304 can be up to about **0.08%**.
  - **316 or 316L Stainless Steel**:
    - Similar to 304 but with added **Molybdenum (Mo)** for **improved corrosion resistance** (especially against chlorides).
    - **316L** has a **lower carbon content** (≤ 0.03%) than 316, which further reduces the risk of corrosion (specifically "intergranular corrosion").
    - Because of its high corrosion resistance and good mechanical properties, 316L is commonly used for **medical implants** (like screws, plates, and some surgical instruments).

- Passivation and Surface Treatment

    - **Passivation**: Creating a **thin oxide layer** on the surface of a metal (often stainless steel or titanium) to **prevent corrosion**.
    - One method is treating the metal with **nitric acid (e.g., ~30%)** to dissolve free iron and help form a stable oxide film. This is crucial for **implants** that need to be highly corrosion-resistant in the body's environment.

- Cold Working
    - **Cold working** (rolling, pressing, forging at low temperature) is a way to **strengthen** metals by **plastic deformation** without the use of high heat.
    - It increases **hardness and tensile strength** but can also make the metal more **brittle**.
    - Cold-worked stainless steels are often used when **high strength** is required (e.g., in certain orthopedic implants).

- Annealing
    - **Annealing** is the process of **heating** a metal and then **slowly cooling** it.
    - This **relieves internal stresses** caused by cold working or other manufacturing processes.
    - Annealed metals are typically **softer and more ductile**, which can be important for forming or shaping parts before final strengthening treatments.

Metals Used in Biomedical Implants

- The notes list common metals for implants:
    - **Fe (Iron), Mo (Molybdenum), Cr (Chromium), Co (Cobalt), Ni (Nickel)**.
- These metals are often alloyed to improve specific properties:
    - **Molybdenum (Mo)**: Enhances **strength** and **corrosion resistance**.
    - **Chromium (Cr)**: Contributes to **corrosion resistance** by forming a **protective oxide layer**.
    - **Cobalt (Co)**: Increases **hardness** and **wear resistance**.

- **Nickel (Ni)**: Improves **toughness** and **corrosion resistance**.

Pitting Corrosion

- **Pitting** ***corrosion occurs when small, localized areas on a metal surface become corroded, leading to tiny holes (pits).*** This is especially problematic for **implants**, as ***it can compromise the integrity of the metal and cause implant failure. Alloying with elements like Cr and Mo helps resist pitting corrosion.***

Surface Properties: Inertness and Smoothness

- **Inertness**: ***The ability of a material to resist chemical reactions, crucial for preventing implant degradation inside the body.***
- **Smoothness**: A smoother surface ***reduces corrosion and bacterial attachment but also influences cell adhesion.***
  - **Mechanotransduction**: ***Cells respond to mechanical cues from the surface. Too smooth or too rough can affect cell attachment and growth.***
  - The goal is to have a ***surface that is smooth enough to resist corrosion but still rough enough to promote cell adhesion.***

Bone Cells and Surface Interaction

- ***When bone cells are placed in a gel, they tend to produce softer tissue rather than forming hard bone.***
- This ***highlights the importance of surface texture and stiffness in guiding bone formation.***

ASTM Standards

- **ASTM (American Society for Testing and Materials)** sets ***standards for materials testing and quality assurance.***
- These standards ensure that ***implants meet safety, strength, and corrosion resistance requirements.***

- ASTM standards are crucial when selecting materials for **medical devices and implants**.

Anodization

- **Anodization** is a process to create a ***thicker oxide layer on the surface of a metal (like titanium or aluminum).***
- It's essentially an ***electrochemical process*** (like an **electrolytic bath**) that ***increases corrosion resistance, wear resistance, and surface hardness.***
- Compared to ***passivation, anodization forms a thicker and more durable oxide layer.***
- This is particularly ***useful for implants that need long-term durability, as it enhances surface protection.***

Surface Interaction and Corrosion Control

- ***The goal is to limit protein and cell adhesion to the metal surface to reduce corrosion, but still allow some level of cell attachment to encourage tissue integration.***
- ***Smooth but not excessively polished surfaces are often preferred to balance corrosion resistance and cell adherence.***

Co-Cr Alloys (Cobalt-Chromium Alloys)

What Are Co-Cr Alloys?

- These are **improved versions of stainless steel 316L**.
- ***They are commonly used in biomedical implants*** ***due to their high strength, corrosion resistance, and biocompatibility.***

Chromium (Cr) in Co-Cr Alloys:

- **Well tolerated by bone cells:**
  - ***Does not harm or kill bone cells, making it safe for biomedical applications.***

        - ***The presence of Cr helps form a protective oxide layer, reducing corrosion and increasing durability.***

Cobalt (Co) in Co-Cr Alloys:

- ***High Concentrations Are Harmful:***
    - Excessive cobalt can be **detrimental to bone cells**.
    - It **lowers collagen I synthesis**, which is essential because:
        - **Collagen I** is the **most prominent extracellular matrix (ECM)** ***protein*** *in bones (about 70%).*
        - It provides structural support and strength.
    - Reduced collagen I synthesis can lead to:
        - **Demineralization:** Loss of mineral content in the bone.
        - **Weakened Bone Structure:** Increased risk of fractures and reduced bone density.

Ti Implants (Titanium Implants)

Purpose:

- Used for ***load-bearing bones due to their strength, lightness, and corrosion resistance.***
- ***Avoid stress shielding, which is when:***
    - ***One bone becomes stronger while adjacent bones weaken.***
    - ***Happens because cells demineralize when stress is not evenly distributed.***
- ***Titanium implants are lighter and reduce stress shielding.***

Ti6Al4V Alloy (Titanium Alloy)

Oxide Layer Formation:

- The body naturally forms a **TiO_2 layer** on the implant surface.
- Over time, this layer becomes a **TiO_2 hydrogel** (a very thin layer).
- The hydrogel helps in the formation of **Hydroxyapatite (HA)**, which:
  - Enhances **bone integration**.
  - Reduces the risk of implant loosening.

Benefits of Ti6Al4V Alloy:

- **Corrosion Resistance:** Due to the oxide layer.
- **Enhanced Osseointegration:**
  - The term **osseointegration** refers to **direct contact between the bone and the implant** without fibrous tissue interference. Promotes **long-term stability** of the implant.

Shape Memory Alloys (SMAs)

- Alloys like **TiNi (Nitinol)** exhibit the **Shape Memory Effect (SME)**:
  - After deformation, they **return to their original shape** when heated.
- **Applications:**
  - Used in **dental braces** to pull teeth into alignment with **body heat**.
  - Also useful in other biomedical devices that require flexibility and shape retention.

Superelasticity

Superelasticity is the ability of a material to undergo large strains and then **return to its original shape** upon unloading.

- **Example:** TiNi (Nitinol)
  - Can **return to its shape after stress is removed**.
  - The graph shows a **stress-strain curve** where TiNi exhibits a loop, indicating **superelastic behavior**.

- **Comparison:** Stainless steel does not show the same superelasticity.

Dental Metals

Gold:

- **Properties:**
  - **Inert, strong, and easily shaped.**
  - Commonly used as **22-carat** (more pure) or **18-carat** (with impurities for strength).

Amalgam:

- **Composition:** A mixture of:
  - **Hg (Mercury)**
  - **Ag (Silver)**
  - **Sn (Tin)**
  - **Fe (Iron)**
  - **Cu (Copper)**
- **Characteristics:**
  - Initially **soft and black**.
  - Becomes **inert and stable** after alloying, despite being toxic on its own.
  - Widely used in **dental fillings** because it becomes **hard and durable** after setting.

Platinum Group Metals (PGMs)

- Includes **Pt (Platinum), Pd (Palladium), Rh (Rhodium), Ir (Iridium)**.
- **Applications:**
  - Often used in **pacemaker tips** and other medical devices due to their **biocompatibility and corrosion resistance**.

Metals in Biomedical Applications

- **Strength and Alloy Forming Ability:** Metals are widely used due to their **high strength** and **ability to form alloys**.
- **Disadvantages:**
  - **Corrosive:** Can degrade over time, especially in a biological environment.
  - **Stress Shielding:** Metals can **distribute stress unevenly**, causing bones to **weaken over time**.
  - **Lack of Bone Mimicry:** Metals do not **mimic the natural properties** of bone, leading to compatibility issues.

Ceramics in Biomedical Applications

Characteristics:

- **Non-metallic, inorganic materials** with **high hardness** and **heat resistance**.
- **Brittle Nature:** Can break easily under sudden forces.
- **Aesthetic Appeal:** Often **smooth and non-reactive**, which reduces **cell adhesion**.
- **Materials Similar to Body Composition:**
  - Examples:
    - **Calcium-based materials** (like Ca and Mg) are **strong but brittle**.
  - **No Stress Shielding:** More similar to bone in terms of stress distribution.

Disadvantages:

- **Microcracks:** Prone to developing **small cracks**, which can **propagate and weaken the structure**.
- **Fragility:** A sudden large force can cause ceramics to **shatter or break**.

Hardness of Ceramics:

- **Hardest Ceramic:** **Diamond (Scale 10)**.

- **Softest Ceramic:** **Talcum Powder (Scale 1)**.
- **General Range:** Mohs hardness scale from **1 to 10**.

Bioceramics:

- Derived from **natural sources** like **shells or corals ($CaCO_3$)**.
- Used for **bone repair and implants** due to their **biocompatibility**.

Types of Ceramics Based on Absorbability:

1. **Non-Absorbable (Relatively Bioinert Bioceramics):**
   - Do not **degrade or resorb** over time.
   - Example: **Alumina, Zirconia**.
2. **Biodegradable (Resorbable) Ceramics:**
   - **Gradually decompose** within the body.
   - Example: **Calcium Phosphate Ceramics**.
3. **Bioactive or Surface-Reactive Ceramics:**
   - Actively **interact with surrounding tissues** to promote **bone growth and bonding**.
   - Example: **Hydroxyapatite (HA)**.

Types of Bioceramics and Their Applications

A) Bioinert Ceramics (Non-Absorbable)

- **Characteristics:**
  - Do not **interact significantly with bone**.
  - **Not absorbed** by the body.
  - No **corrosion**, but can undergo **wear and tear**.
- **Examples:**

1. **Alumina (Al_2O_3)**:
    - Highly **structural and durable**.
    - Used in **bone plates**, **femoral heads**, **middle ear ossicles**, and **hip joints**.
    - **Sapphire** is a natural form of alumina.
2. **Zirconia**:
    - Similar applications as alumina.
    - Known for **high strength and toughness**.

B) Bioactive and Resorbable Ceramics (Biodegradable)

- **Characteristics:**
    - **Degrade gradually** in the body.
    - Components are **absorbed and utilized**.
- **Examples:**
    1. **Coralline (made from corals)**:
        - Contains **Hydroxyapatite (HA)** and **Tri-Calcium Phosphate (TCP)**.
        - Often used for **artificial bones** or to **fill bone defects**.
        - The **Ca:P ratio is typically 1.6**, similar to natural bone.
    2. **Plaster of Paris**:
        - Used for **bone defects or fractures**.
    - **Hydroxyl Group**: Reacts with **water** to set and **mineralize bones**.

C) Bioactive or Surface-Reactive Ceramics

- **Characteristics:**
    - **Interact with surrounding cells** and environment.
    - Influence **bone growth and integration**.
- **Example:**

- **Pyrolytic Carbon**:
  - Used to make **coatings for implants**.
  - **Inert and very strong**.
  - Often combined with **polymers** for added flexibility and corrosion resistance.
  - Example: **TiNi coated with PLC** to prevent corrosion.

Mechanical and Physical Replacement

- Used for **structural support**.
- Materials like **Alumina and Zirconia** serve as **load-bearing implants**.

Shape Memory Alloys (SMAs) in Biomedical Applications

- **TiNi Alloy (Nitinol)**:
  - Can **return to its original shape** after deformation.
  - Used in **stents and angioplasty**.
- **Application in Stents**:
  - **Shape Memory Effect**: Allows stents to expand after being inserted.
  - **Angioplasty**: Helps to **keep arteries open** and **reduce blood pressure**.

Additional Concepts

- **Angioplasty and Stenting**:
  - Involves **inflating a balloon to open a blocked artery**.
  - The **stent holds the artery open** to maintain blood flow.
- **Occlusion by Fatty Acids**:
  - Blockages can occur due to **fat deposition**, causing **increased blood pressure (BP)**.

Liquidation of Ceramics and Its Applications

Liquidation of Ceramics:

- **Purpose:**
  - To **reduce sensitivity** by making **enamel harder**.
  - Used in **bone trauma**, **drug delivery**, and **dental applications**.
  - **Ability to hold drugs** in ceramics.

Types of Ceramic Materials

1) ALCAP (Aluminum Calcium Phosphate)

- **Composition:**
  - Aluminum and Calcium Phosphate.
  - Form: **Powders and cylinders**.
- **Application:**
  - Used as **biomaterials** for bone repair.

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2) FECAP (Iron Calcium Phosphate)

- **Composition:**
  - Derived from **Calcium Phosphate** with **Iron**.
- **Application:**
  - **Iron deficiency treatments**.

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3) Biocoraline

- **Origin:**
  - Derived from **marine organisms**.
  - Composition: **$CaCO_3$** (Calcium Carbonate).
- **Characteristics:**
  - **Porous** nature, allows **nutrient flow**.

- **Strength:** 400–500 MPa, comparable to bone.
- **No stress shielding.**

- **Applications:**
  - Used to **repair bone defects**.

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4) TCP (Tri-Calcium Phosphate)

- **Composition:**
  - Contains **$Ca_3(PO_4)_2$**.
- **Application:**
  - Used as **bone graft material**.

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5) ZCAP (Zinc Calcium Phosphorous Oxide)

- **Composition:**
  - **Zinc, Calcium, and Phosphorous Oxide**.
- **Application:**
  - Used in **bone regeneration**.

Bioactive/Surface Reactive Ceramics (Type C)

Key Concept:

- These ceramics **interact with surrounding tissues** and promote **biological integration**.

Cell Types Involved in Bone Integration:

1. **Osteoclasts:**
   - **Function:** Break down and **resorb bone**.
   - **Action:** Clear out damaged bone.
2. **Osteoblasts:**

- **Function: Build new bone** by laying down mineralized matrix.

3. **Osteocytes:**
   - **Function:** Maintain the **bone tissue**.
   - **Action:** Sense mechanical stress and **signal for repair**.

Bone Healing Process:

1. **Blood Clot Formation:**
   - Bone cells migrate to form a **clot** at the damage site.
2. **Bone Cell Migration:**
   - Osteoblasts migrate to **deposit new minerals**.
3. **Bone Remodeling:**
   - Osteoclasts remove the old bone, and **osteoblasts build new tissue**.

Bioglass (Bioactive Glass):

- **Composition:**
  - Contains **SiO_2, CaO, Na_2O, P_2O_5**.
- **Advantages:**
  - **Activates cells biologically**, allowing **stress distribution**.
  - **Smooth and strong** surface, minimizing friction and stress shielding.

Hairline Fractures:

- **Definition:**
  - Small cracks in bones that may develop due to **repetitive stress**.
- **Healing Role of Bioactive Ceramics:**
  - They **activate osteocytes and osteoblasts**, promoting **quick healing and mineralization**.

Creating Porosity in Ceramics for Bone Cell Integration

Why Porosity is Important:

- Bone cells need **space to move inside** the ceramic structure.
- Porosity allows for **cell migration**, **nutrient flow**, and **vascularization**.

Methods to Introduce Pores in Ceramics:

1. **Starch Consolidation:**
    - **Process:**
        - Mix **ceramic powder** with **starch** and **fire** the mixture.
        - During firing, **starch burns out**, leaving **pores**.
    - **Advantages:**
        - **Controlled porosity** based on starch concentration.
    - **Applications:**
        - Commonly used in **bone graft materials**.

1. **Dip Coating:**
    - **Process:**
        - Ceramic material is **mixed with air** and **heated** to high temperatures.
        - **Air bubbles get trapped**, forming **pores**.
    - **Advantages:**
        - More **consistent porosity** than starch consolidation.
        - Suitable for **coating medical implants**.

Comparing Both Methods:

- Starch consolidation allows **variable porosity**.
- Dip coating produces **uniform pores**.
- Choice of method depends on **desired pore structure and application**.

Polymers: The Flexible and Versatile Material

Advantages of Polymers:

- **High Flexibility and Strength:**
  - Adaptable to **various shapes and movements**.
- **Tunable Properties:**
  - **Adjustable molecular weight** and **chain structure** for flexibility or rigidity.
- **Easy Synthesis:**
  - Can be **easily scaled** and **customized**.
- **Biological Interaction:**
  - Functional groups can be added for **biocompatibility**.
- **Lightweight and Affordable:**
  - Ideal for **medical applications** like **heart valves and synthetic blood vessels**.

Common Polymer Example: PVC (Polyvinyl Chloride)

- **Properties:**
  - **Durable**, **flexible**, and **easily shaped**.
- **Uses:**
  - Medical tubing, catheters, and **flexible implants**.

Polymer Chain Structures:

1. **Long Chains (Rigid & Dense):**
   - **High strength**, but **less flexible**.
   - **Example:** High-density polyethylene (HDPE).
2. **Short Chains (Compact):**
   - **Lower strength**, but **more flexible**.

- **Example:** Low-density polyethylene (LDPE).

3. **Combination of Long and Short Chains (LC + SC):**
   - **Balanced strength and flexibility**.
   - Suitable for **load-bearing implants**.

Molecular Weight and Its Impact:

- **Higher Molecular Weight:**
  - Increases **strength** and **stiffness**.
- **Lower Molecular Weight:**
  - Increases **flexibility** and **elasticity**.

Applications in Medicine:

- **Heart Valves:**
  - Need to be **both strong and flexible** to withstand continuous movement.
- **Synthetic Blood Vessels:**
  - Require **strength** for pressure resistance and **flexibility** to mimic natural vessels.

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1. Polymer Degradation & Drug Delivery

- **What happens when polymers degrade?**

  When polymers break down, the materials can be **utilized by the body**. This is crucial in medical applications like **biodegradable implants or drug delivery systems**.

- **Application in Drug Delivery:**
  - Degrading polymers can **release drugs** at a controlled rate.
  - This helps in **sustained drug release** inside the body.
  - Example: **Biodegradable sutures** or **drug-eluting stents**.

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2. Size of Functional Groups & Their Effects

- **Big/Bulky Functional Groups:**
  - Cause **limited deformation (def. saturation limited)**.
  - Create **more gaps** in the structure.
  - Makes the material **viscous & soft**.
- **Small Functional Groups:**
  - Pack **more compactly**.
  - Increase **strength** of the material.

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3. Branching in Polymers

- **Effect of Branching:**
  - Leads to **tight bounding** due to **cross-bridging**.
  - This improves **structural integrity** and **mechanical strength**.
  - Example: **Crosslinked polymers like vulcanized rubber**.

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4. Spider Silk Properties

- **Spider silk is extremely strong**—even stronger than steel by weight!
- **Why?**
  - It has a **well-organized protein structure** with many **β-sheets**.
  - These sheets form **more bonds**, storing **more energy** per bond.
- **Structural Components:**
  - **α-helix & loops** → Provide **extensibility** (ability to stretch).
  - **β-sheets** → Provide **strength**.
- **Keratin vs. Spider Silk:**
  - **Keratin (in hair/nails):** More flexible but still strong.
  - **Spider silk:** Similar to β-keratin but has better **energy distribution**, making it **tougher and more resilient**.

Ordered vs. Random Structures in Polymers

- **Ordered (Crystalline) Structures**
  - More **compact** → Stronger
  - More **stable** due to better molecular packing
- **Random (Amorphous) Structures**
  - Less **compact** → Weaker
  - More susceptible to **degradation**

👉 **Example:** Crystalline regions in polymers like nylon make them strong, while amorphous regions make them flexible.

Common Polymers & Their Properties

PVC (Polyvinyl Chloride)

- **Properties:**
  - Strong, flexible
  - Contains **both long & short chains**
  - **Short chains** act as **plasticizers**, reducing **viscosity** (fluidity)
  - Stabilizers (salts) are added to **slow down deterioration**
- **Why isn't PVC used in the body?**
  - Contains **bulky chlorine (Cl)**
  - When combined with water, it forms **HCl (hydrochloric acid)** → **toxic**

Polyethylene (PE)

- Different types of polyethylene vary in **density & molecular weight**:
  - **LDPE (Low-Density PE)** → Flexible
  - **HDPE (High-Density PE)** → Stronger, rigid

- **LLDPE (Linear Low-Density PE)** → More flexible than LDPE
- **VLDPE (Very Low-Density PE)** → Very soft, stretchable
- **UHMWPE (Ultra High Molecular Weight PE)** →
  - **Very strong & heavy**
  - Used in bulletproof vests and high-performance gears

PMMA (Polymethyl Methacrylate)

- **pH resistant**
- **Transparent**
- Used in **contact lenses** due to its clarity and biocompatibility

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Polystyrene (PS)

- Different types:
  - **GPPS (General Purpose Polystyrene)** → Basic applications
  - **HIPS (High-Impact Polystyrene)** → More durable
  - **PS Foam (Polystyrene Foam)** → Used in packaging (e.g., Styrofoam)

Nylon (Polyamide)

- Has **both crystalline & amorphous regions**
- **Breaks down due to hydrolysis**, especially in **amorphous regions**
- Commonly used in **textiles, ropes, and engineering plastics**

Summary

- **Crystalline structures** → Stronger, more stable
- **Amorphous structures** → Weaker, degrade faster
- **PVC is strong & flexible but toxic in the body**
- **Polyethylene types vary in strength & density**

- **PMMA is transparent & used in contact lenses**
- **Polystyrene is used in different forms, including foam**
- **Nylon is strong but breaks down in water over time**

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1. Aromatic Polymers (ARAMIDS)

- **Example: Kevlar** (inspired by spider silk)
  - **5 times stronger than steel**
  - **Lightweight**
  - **Woven structure** helps in shock absorption
  - Used in **bulletproof vests, aerospace, and high-strength applications**

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2. Rubber

- **What is Rubber?**
  - A tree sap that **solidifies** when exposed to air.
- **Natural Rubber**
  - Used in **biomedical applications**.
  - **Blood-compatible, flexible & elastic**.
  - **Vulcanization** → Adding **sulfur** makes rubber **stronger & more durable**.

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3. PDMS (Polydimethylsiloxane)

- **Synthetic silicone-based polymer**
- **Applications**:
  - **Lubricants, coatings for medical devices**
  - **Microfluidics** (used in lab-on-a-chip devices)
  - **Insulin reservoirs inside the body** for **Type 1 diabetes**

---

4. Polyurethane (PU)

- **Used for coatings & biomedical applications**
- **Prevents corrosion**

---

5. Biodegradable Polymers

These are used in **medical applications** where the material needs to degrade inside the body.

- **Poly Lactic Acid (PLA)**
  - **Degradable**
  - **Mimics the body** (biocompatible)
- **Poly Glycolic Acid (PGA)**
  - **Used in medical sutures** (only small quantities needed)
  - Too much can be **toxic** (pH changes can kill cells).
- **PLGA (Poly Lactic-co-Glycolic Acid)**
  - **Blend of PLA & PGA** → Improves degradation control.

---

6. Disadvantages of Biodegradable Polymers

- **Uncontrolled degradation** can cause unexpected failures.
- **Sterilization issues**:
  - **Some materials can't withstand common sterilization methods.**
  - **Different Sterilization Techniques:**
    - **Dry heat** (160–190°C)
    - **Wet heat (autoclaving)** (125°C)
    - **Radiation** (gamma rays, UV)
    - **Chemical sterilization** (alcohol, ethylene oxide)
  - Some **plastics become brittle** or **toxins are released** after sterilization.

---

7. Microfluidics

- **Why is it useful?**
  - Simulates **biological environments** on a smaller scale.
  - **Requires less sample volume**, making experiments more efficient.
  - Used in **medical diagnostics, lab-on-a-chip technology**.
- **Application in Type 1 Diabetes**
  - Helps in developing **miniaturized insulin delivery systems**.

Summary

- **Kevlar (aramids) → Super strong, lightweight, used in bulletproof vests.**
- **Rubber → Elastic, biocompatible, improved via vulcanization.**
- **PDMS → Used in lubricants, microfluidics, insulin reservoirs.**
- **Polyurethane (PU) → Prevents corrosion.**
- **Biodegradable polymers (PLA, PGA, PLGA) → Used in medical implants, but degradation needs control.**
- **Microfluidics → Important for medical research and diagnostics.**

---

1. What are Composites?

- **Definition:** Composites are materials made from two or more distinct components that maintain their individual chemical identities but work together to provide improved properties.
- **Why use composites instead of just polymers?**
  - Polymers generally have **low strength**.
  - Composites **enhance strength** while being **lighter** than metals.
  - They can be **stiff, strong, and lightweight**.

---

2. Components of Composites

- **Composites must have at least two components**:
  - **A matrix** (continuous phase) that binds everything.
  - **A reinforcement** (dispersed phase) that provides strength.
- **Examples**:
  - **Foam** = Air + Polymer
  - **Food** (Certain structured food items act as composites)
  - **Sponge** = Air + Sponge material
  - **Bone** = Many elements combined to give strength
  - **Concrete** = Cement + Sand + Gravel
- **Comparison with other materials**:
  - Strength similar to **steel** but lighter than polymers.

---

3. Composite Structure

The structure of a composite affects its properties.

(A) Shape Decides Outcome

Different reinforcement shapes lead to different properties:

1. **Particle (No long dimension)**
   - Randomly distributed in the matrix.
   - Provides **isotropic** properties (same strength in all directions).
2. **Fiber (1D Reinforcement)**
   - Provides **high strength** in the direction of fibers.
   - Examples: Carbon fiber, fiberglass.
3. **Platelet (2D Reinforcement)**
   - Can provide layered strength.
4. **Laminar (Layered structure)**
   - Used in laminated composites like plywood.

- **Voids (empty spaces in composite)**:
  - More voids = **less strength**.
  - Good compaction reduces voids.
  - Smaller particles **fill gaps**, improving strength.

(B) Volume Fraction

- **Definition:** The proportion of each component in the total composite volume.
- **Importance:** A higher reinforcement fraction usually means better strength.

---

4. Practical Example: Concrete

- **Components**:
  - Cement (matrix)
  - Sand + Stone chips (reinforcement)
- **Why is it strong?**
  - Gravel + sand fill gaps, reducing voids.
  - Proper compaction improves load distribution.

Key Takeaways

1. Composites **combine two or more materials** to create a stronger, lighter material.
2. The **type of reinforcement** (particle, fiber, platelet, laminar) affects the properties.
3. **Minimizing voids** and using a **good volume fraction** enhances strength.
4. **Concrete** is a common composite with strong load-bearing properties.

---

1. Interface in Composites

- **Definition:** The interface is the region where different components of a composite come in contact.

- **Why is it important?**
  - It affects how well the different materials **stick together**.
  - Poor interfacing leads to **weak bonds** and **breakage**.
- **Composites are resistant to breakage** due to the presence of **fibers** which enhance their mechanical properties.

Examples of Interfaces in Materials:

- **Foam:** Made of **polyhedral** cells.
- **Sponge:** Has **voids** (empty spaces).
- **Honeycomb:** A structure with repeated **hexagonal cells**.

Heterogeneous vs. Homogeneous Materials

- **Heterogeneous materials** have **more unique properties** and better **multidirectional performance**.
- **Homogeneous materials** (like particle-based composites) have **less functionality** because their properties are uniform.

---

2. Weight and Reuss Structures

- **Weight structures**:
  - The **strain** is the same across all components.
  - Example: In a composite material, if strain is distributed equally, it behaves as a **single unit**.
- **Reuss structures**:
  - The **stress** is the same across all components.
  - This is often used in **layered composites** where different materials bear the same amount of force.

---

3. Composite Strength Formulas

(A) Voigt Model (for Strength)

This formula calculates the **effective Young's modulus** (E) when strain is the same across components:

$$E = E_i V_i + E_m(1 - V_i)$$

Where:

- E_i = Young's modulus of inclusion (reinforcement)
- E_m = Young's modulus of matrix
- V_i = Volume fraction of inclusion

(B) Reuss Model (for Stiffness)

Used when stress is the same across components:

$$E = \left(\frac{V_i}{E_i} + \frac{1 - V_i}{E_m} \right)^{-1}$$

This formula is useful in materials where flexibility and load distribution are key factors.

---

4. Anisotropy in Composites

- **Definition:** Anisotropy means a material has **different properties in different directions**.
- **Why is it important?**
  - The **more anisotropic & heterogeneous** a composite, the **better its performance**.
  - Example: **Carbon fiber composites** have high strength in one direction but may be weaker in others.

---

5. Practical Example: Rubber Soles

- **Rubber soles** in shoes are composites with **added particles**.
- These **increase strength and durability** compared to pure rubber.

Key Takeaways

1. **Interface strength** is crucial in composites for durability.
2. **Heterogeneous composites** have better performance than homogeneous ones.
3. **Voigt and Reuss models** help in predicting composite material behavior.
4. **Anisotropy** leads to better-designed, superior products.
5. **Rubber soles and other common materials** use composite principles for improved properties.

Would you like a **detailed example** of any concept? 😊

POST QUIZ

Drug Delivery

This is the overall process of administering a pharmaceutical compound to achieve a therapeutic effect in humans or animals.

- **Conventional Drug Delivery**

  These systems release the drug immediately and are not designed to control the rate or location of drug release.

  - **Enteral:** Drug is delivered via the gastrointestinal tract (e.g., oral, sublingual, rectal).
  - **Parenteral:** Drug is delivered through injections, bypassing the GI tract (e.g., intravenous, intramuscular).
  - **Other:** May include topical, nasal, or inhalational routes.

- **Controlled Drug Delivery**

  These systems are designed to release drugs at controlled rates or at specific sites.

  - **Sustained:** Drug is released slowly over time to maintain a steady concentration.
  - **Extended:** Prolongs the release of the drug, reducing the frequency of dosing.
  - **Site-specific:** Delivers the drug to a targeted location in the body.
  - **Pulsatile:** Releases the drug in bursts at specific times, mimicking physiological needs.

Capsules:

- **Form**: A gelatin shell (either hard or soft) filled with the drug in powder, liquid, or semi-solid form.
- **Types**:
  - **Hard gelatin capsules**: Usually contain dry powdered drugs.
  - **Soft gelatin capsules (softgels)**: Often filled with oils or liquid drugs.
- **Disintegration**: Gelatin shell dissolves quickly in the stomach, releasing the contents.
- **Advantages**:

    - Easier to swallow for many people.
    - Can hold unpleasant-tasting/smelling drugs.
    - Faster drug release than tablets (usually).
- **Disadvantages**:
    - Less stable in hot/humid conditions.
    - Often more expensive to manufacture.

Tablets:

- **Form**: Solid compressed form of the drug, often with excipients (binders, fillers, etc.).
- **Types**:
    - Coated, uncoated, chewable, effervescent, etc.
- **Disintegration**: Breaks apart in the stomach to release the drug.
- **Advantages**:
    - Stable and has a longer shelf life.
    - More cost-effective to produce.
    - Can be split into halves (if scored).
- **Disadvantages**:
    - Harder to swallow for some.
    - Slower onset compared to capsules.

Other Traditional Oral Systems (as you listed):

- **Soft gelatin capsules**: Liquid-filled, fast absorption.
- **Suspensions**: Drug particles suspended in liquid; shaken before use.
- **Elixirs**: Sweetened, alcohol-based solutions used for flavor and solubility.

What is "Bypass First Pass Metabolism"?

When a drug is taken **orally (swallowed)**, it travels through the **digestive system**, then to the **liver** via the **portal vein** before entering systemic circulation. This is called **first-pass metabolism**, and it can significantly reduce the drug's effectiveness by breaking down a large portion of it in the liver.

👉 **Bypassing first-pass metabolism** means the drug **enters the bloodstream directly**, skipping the liver's filtering stage initially — leading to **faster** and often **more effective** drug action.

🧪 What is Oral-Lyn?

- **Form**: A **liquid formulation of human insulin**.
- **Delivery Route**: Administered through the **buccal mucosa** (inside the cheek).
- **Method**: Delivered via **aerosolization** — the patient sprays the insulin into their mouth.
- **Technology**: The drug is **carried in lipid micelles**, which help with absorption through the buccal tissue.

💡 Why Buccal Delivery for Insulin?

- Normally, insulin is injected because it **breaks down in the stomach** if swallowed.
- Buccal delivery **bypasses the digestive system** and **first-pass metabolism**, allowing insulin to enter directly into the bloodstream.
- It's **non-invasive**, convenient, and quick-acting.

📈 Graph: Glucose Level Over Time

- The graph compares **Oralin 45a** (Oral-Lyn) and **Humulin** (traditional injectable insulin).
- **X-axis**: Time in minutes
- **Y-axis**: Glucose levels (mg/dL)

🔵 Oralin 45a (blue line):

- Slower onset compared to Humulin initially.
- Gradual and prolonged reduction in glucose levels.
- Suggests **extended effect**, potentially beneficial for sustained blood sugar control.

🟣 Humulin (pink line):

- Faster drop in glucose level, peaking earlier.
- Shorter duration of action.
- **Rapid onset**, but **not as prolonged** as Oralin.

✅ Takeaway:

Oral-Lyn shows that **buccal aerosol insulin** is a **viable alternative** to injections, with **potential for better patient compliance** and **steady glucose control**, thanks to its **non-invasive and extended delivery profile**.

🧪 1. Physicochemical Properties of the Drug

These influence **how the drug behaves in the body** and determine which routes are feasible:

Factor	Explanation
Solubility	Hydrophilic drugs prefer aqueous environments (e.g., IV), while hydrophobic drugs may need lipid-based carriers.
pH & pKa	Affects ionization and drug absorption across membranes; ideal absorption occurs when drugs are in unionized form.
Temperature	Influences stability and solubility; some formulations require refrigeration or body-temperature activation.
Concentration	High drug concentration may require specialized delivery forms to avoid toxicity.
Crystallinity	Impacts solubility; amorphous drugs generally dissolve faster than crystalline forms.

Particle Size	Affects absorption rate, especially in suspensions or inhalables.
State of Hydration	Hydrated vs. anhydrous forms affect drug dissolution and bioavailability.

🔄 2. Drug–Biological Interactions

These determine **how the drug interacts with the body** and its effectiveness:

Factor	Explanation
First-pass metabolism (FPM)	Drugs sensitive to liver metabolism may be better delivered via buccal, IV, or nasal routes.
Membrane permeability	Low permeability drugs need delivery systems that enhance transport (e.g., liposomes).
Efflux pumps (MRP, MDR)	Seen in cancer, where drugs are pumped out of cells, reducing efficacy.
Hydrophilicity	Poor lipid membrane passage, affecting oral and transdermal delivery.
High-density charge	Limits cell membrane passage due to electrostatic repulsion.
Enzymatic/Bacterial degradation	Drugs broken down by enzymes or gut flora may need protective coatings or alternative routes.
Half-life	Short half-life drugs may require sustained or controlled-release systems.
Side effects / Irritation	Irritating drugs may be unsuitable for certain mucosal routes.

🎯 3. Desired Pharmacological Effect

These relate to **what you want the drug to do**, and how fast or where it should act:

Factor	Explanation
Local effect	Routes like topical or vaginal are chosen when local action is needed.
Systemic effect	Routes like oral, IV, IM, buccal, or nasal are used for whole-body effects.

Immediate response	Routes like IV, IM, SC, and nasal provide quick onset of action.
Dose size	Large doses may not be suitable for small-volume routes (e.g., nasal, buccal).
Molecular size	Large molecules (e.g., proteins) may not be absorbed orally; need injection or specialized carriers.

Manufacture of Classical Oral Drug Delivery Systems

🔬 1. Formulation

- The **formulation** is the process of **combining the active pharmaceutical ingredient (API)** with various **excipients** to create a usable, effective, and stable drug product. The goal is to ensure the drug delivers the **intended therapeutic effect** with the right **release profile**, **stability**, and **patient acceptability**.

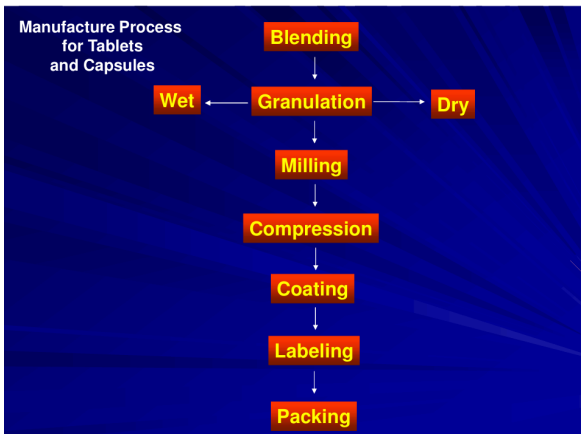
⚗️ 2. Excipients (Inactive Ingredients)

Excipients are **non-medicinal substances** added during drug manufacturing to help with formulation and delivery. They play **critical roles**, even though they don't have therapeutic effects themselves.

💡 Functions of Excipients:

Function	Purpose
Dilution (Fillers)	Add bulk to tablets or capsules for accurate dosing.
Protection	Protect the active ingredient from degradation (light, air, moisture).
Stability	Maintain the drug's effectiveness during shelf life.
Controlled Release	Modify how fast or where the drug is released in the body.
Taste Masking	Improve patient compliance by masking bitter flavors.
Disintegration	Help the tablet break apart after ingestion for faster release.

Coloring/Coating	Aid in identification, branding, or improve appearance.



💊 Manufacture Process for Tablets and Capsules

1. Blending

- **What happens:** All ingredients (active drug + excipients) are **uniformly mixed**.
- **Why it matters:** Ensures each tablet/capsule contains the right amount of active drug.

2. Granulation

- **Purpose:** Converts powders into **larger, free-flowing granules**.
- **Two types:**
  - **Wet granulation:** Uses a liquid binder to agglomerate the powder.
  - **Dry granulation:** Compresses powder without using liquids, often via slugging or roller compaction.
- **Why granulation:** Improves **flowability**, **compressibility**, and **uniformity**.

3. Milling

- **What happens:** Granules are **sized and refined** for uniform particle distribution.

- **Purpose:** To achieve proper size for optimal tablet strength and smooth capsule filling.

4. Compression

- **Tablets:** Granules are pressed into **solid tablets**.
- **Capsules:** Granules are filled into **hard gelatin capsules**.
- **Key point:** Precise force and die shape control size and hardness.

5. Coating

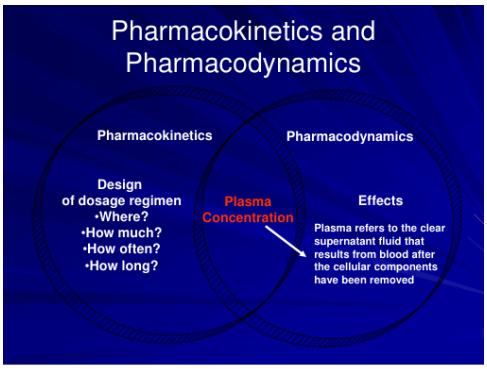
- **Purpose:** Apply a protective or functional layer (e.g., taste-masking, delayed-release).
- **Types of coatings:** Film coating, sugar coating, enteric coating.

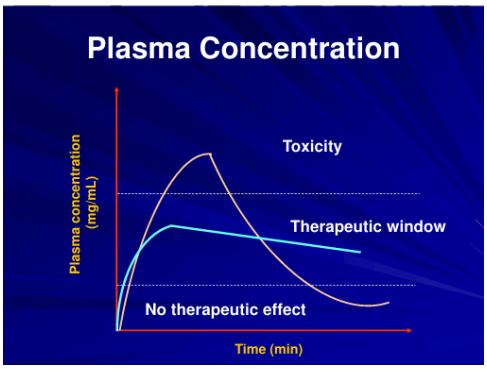
6. Labeling

- **Step:** The tablets/capsules are **identified and branded** with necessary information (e.g., dosage, brand name, manufacturer).

7. Packing

- **Final step:** Finished products are **packaged** in blister packs, bottles, etc., for distribution.





🔄 Pharmacokinetics vs. Pharmacodynamics (Top Diagram)

These two fields describe what a drug does in the body—and what the body does to the drug.

🔷 Pharmacokinetics ("What the body does to the drug")

- Focus: **Absorption, distribution, metabolism, and excretion (ADME)**
- Questions it answers:
  - **Where** does the drug go?
  - **How much** should be given?
  - **How often** should it be administered?
  - **How long** will it stay active?

🔷 Pharmacodynamics ("What the drug does to the body")

- Focus: **Drug effects on the body**
- Includes **mechanism of action, receptor interactions**, and **side effects**

🔶 Shared Middle: Plasma Concentration

- Both fields rely on **plasma drug levels**:
  - Determines whether the drug reaches effective or toxic levels.
  - Guides dosage design **(Pharmacokinetics)** and predicts response **(Pharmacodynamics)**.

📈 Plasma Concentration vs. Time (Bottom Graph)

This graph illustrates the **therapeutic window**—the safe and effective range for drug concentration in the blood.

🔷 Axes:

- **Y-axis:** Plasma concentration (mg/mL)
- **X-axis:** Time (minutes)

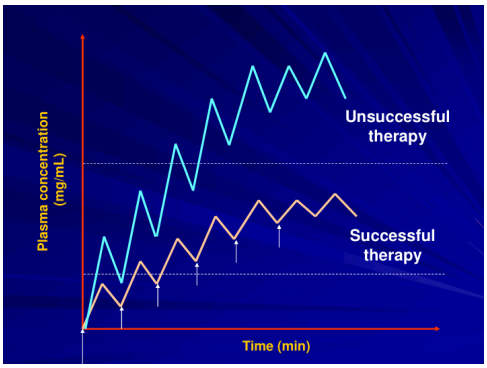
🔶 Three Zones:

1. **No Therapeutic Effect** (Below minimum effective concentration)
   - Drug levels too low to produce desired outcome.
2. **Therapeutic Window**
   - Optimal zone for effect without toxicity.
   - Goal: Keep plasma concentration in this range.
3. **Toxicity**
   - Drug levels too high → Side effects or harm.

🔶 Curves:

- Represent different dosing regimens or formulations.
  - A **sharper peak** may mean faster onset but higher risk of toxicity.

- A **flatter curve** shows controlled release—safer and longer duration.



Magnitude of Drug Response
Depends upon concentration achieved at
- the site of action

– Dosage

– Extent of absorption

– Distribution to the site

– Rate/extent of elimination

🧭 1. Drug Delivery

This is the **first step**—how the drug gets into the body.

- **Route of Delivery**:
  - Oral, intravenous (IV), intramuscular (IM), sublingual, etc.
- **Key Considerations**:
  - **Physicochemical properties** of the drug (e.g., solubility, pKa, size)
  - **Design of dosing regimen**:
    - How much?
    - How often?
    - For how long?

🧪 2. Absorption

Once administered, the drug must **enter the bloodstream** (except IV which directly enters blood).

- **Factors Influencing Absorption**:
  - **First pass metabolism**: Especially for oral drugs, where liver metabolizes drug before systemic circulation.
  - **Membrane barriers**: Drug must cross biological membranes.
  - **Efflux pumps**:
    - **MDR (Multi-Drug Resistance)**
    - **MRP (Multi-drug Resistance-associated Protein)**
    - These pumps may actively remove the drug from cells, reducing effectiveness.

🔁 3. Distribution

After absorption, the drug **moves throughout the body** to reach its site of action.

- **Targets**:
  - **Tissues** (e.g., lungs, brain)
  - **Plasma** (systemic circulation)
- Influenced by:
  - **Blood flow**
  - **Binding to plasma proteins**
  - **Molecular size and lipophilicity**

🧹 4. Elimination

The drug is eventually **removed from the body**, either unchanged or as metabolites.

💥 Metabolism:

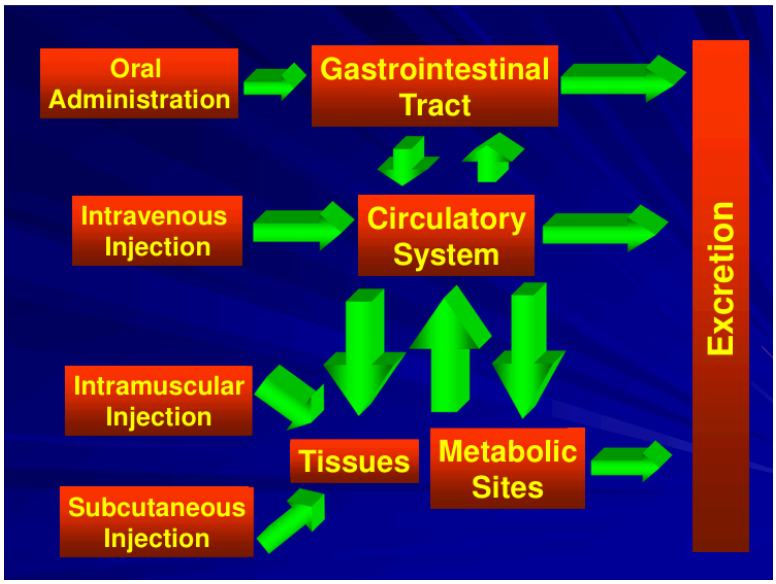
- Usually happens in the **liver** (via enzymes like CYP450).
- Converts drug into more water-soluble forms for easier excretion.
- May activate (prodrugs) or deactivate the drug.

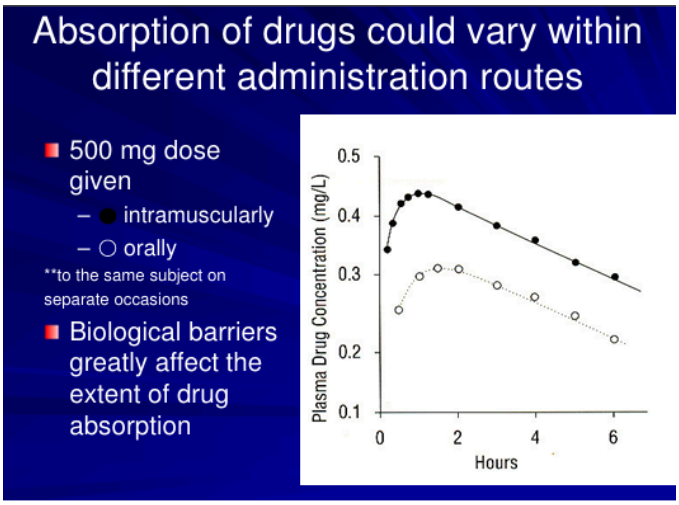
🚽 Excretion:

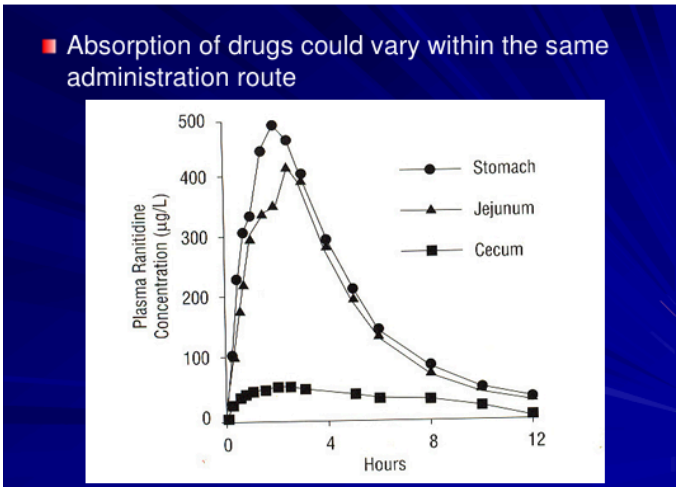
- **Kidneys** (primary route): Drug/metabolites exit via urine.
- **Feces**: Through bile secretion into the GI tract.
- Minor routes: sweat, saliva, breath.

🧩 Summary

Phase	Key Concept	Organs/Systems Involved
Delivery	Getting drug into the body	Oral/GI tract, veins, etc.
Absorption	Into bloodstream	GI tract, membranes
Distribution	To site of action	Bloodstream, tissues
Elimination	Out of the body	Liver (metabolism), kidneys (excretion)







Mathematical Modeling of Drug Disposition
Single compartment
Single compartment with absorption
Two compartments
Two compartments with absorption
Physiological Models

💊 1. Single Compartment Model

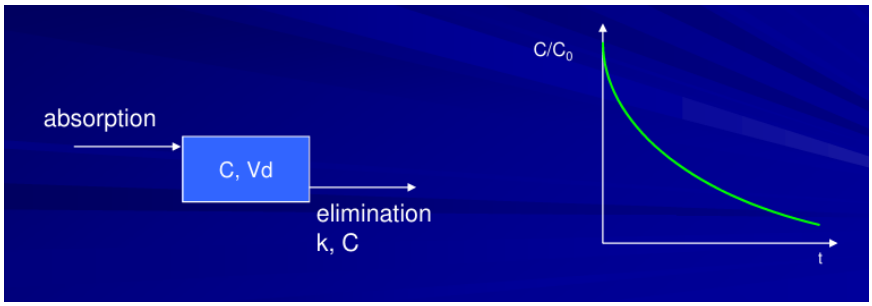
📌 Assumptions:

- The body is treated as **one uniform compartment**.

- The drug is **evenly distributed** throughout the plasma.
- No absorption phase (assumes **instant IV injection**).
- **Volume of distribution (Vd)** is constant.

🧠 Use Case:

Good for **simple drugs** that stay in the bloodstream and don't spread into tissues.



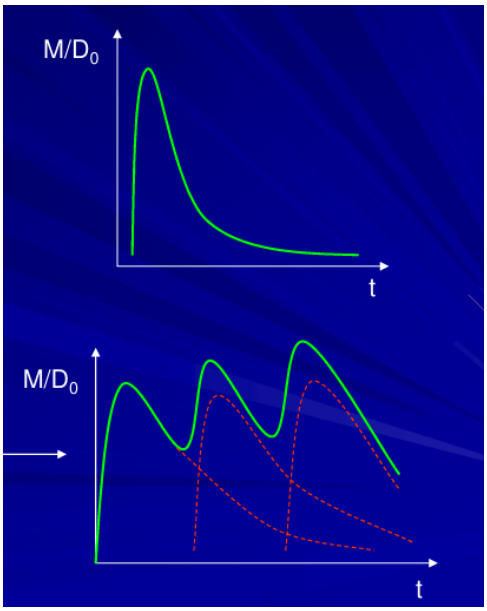
🧪 2. Single Compartment with Absorption

📌 Key Features:

- Drug must **absorb into plasma first**, typically from **oral** or **subcutaneous (SC)** delivery.
- **Absorption is the rate-limiting step** (e.g., drug enters blood slowly).
- Once absorbed, it's still treated as one compartment.

🧠 Use Case:

- Drugs given **orally or via SC injection**.
- **Slow-release** medications or drugs that don't immediately hit the bloodstream.
- Requires **multiple doses** to maintain effective concentration.



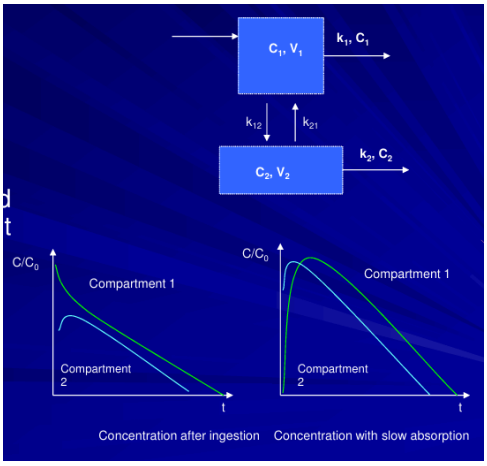
🔁 3. Two-Compartment Model

📌 How it works:

- The body is split into:
  - **Central compartment** (e.g., blood/plasma)
  - **Peripheral compartment** (e.g., tissues/organs)
- Drug is **rapidly distributed** in the central compartment after injection.
- Then it **slowly moves** into and out of the peripheral compartment.

🧠 Use Case:

Used for **drugs that distribute into tissues** and don't stay in the bloodstream.



🧬 4. Two-Compartment with Absorption

- Combines both **distribution** and **absorption** dynamics.
- Represents more **realistic** drug behavior in the body, especially for **oral drugs that also distribute widely**.

🧠 5. Physiological Models

- Most complex and **realistic**.
- Treat each **organ/tissue** as its own compartment.
- Incorporate **anatomical and physiological** data (like blood flow, organ size, metabolic rate).

🧠 Use Case:

- **Precision modeling** in drug development and research.
- Predicting **human responses** based on **animal models**.

Summary Table:

Model Type	Key Features	Use Case
Single Compartment	Instant IV, drug in plasma only	Fast-acting IV drugs

Single Compartment + Abs.	Absorption required, slower entry	Oral or SC meds needing steady state
Two-Compartment	Distribution into tissues	Drugs with tissue storage (e.g., fat-soluble)
Two-Compartment + Abs.	Absorption + distribution	Complex kinetics
Physiological Model	Based on actual organs and physiology	Research, modeling across species

✅ Determination of Efficacy of the Delivery Route

💡 Bioavailability (F)

- **Definition:** The **fraction** of an administered drug that reaches **systemic circulation** in an **active form**.
- For **oral drugs**, some is lost due to digestion and **first-pass metabolism**, so F < 1.
- For **IV drugs**, F = 1 (100%) because it's delivered directly into the bloodstream.

📖 FDA Definition (Food, Drug, and Cosmetic Act):

> "The rate and extent to which an active ingredient is absorbed and becomes available at the site of action. If the drug isn't meant to enter the bloodstream, other markers are used to measure bioavailability."

🔬 Factors That Influence Bioavailability:

1. **Delivery route** (oral, IV, IM, etc.)
2. **Site of measurement** (plasma, target tissue, etc.)
3. **Species used in trials** (rat vs. human)
4. **Physiological state**:
    - Illness (e.g., kidney or liver dysfunction)

- Use of **anesthesia** (which may alter metabolism)

🧠 Implications of PK/PD in Drug Delivery

PK = What the body does to the drug

PD = What the drug does to the body

- **Route of administration** affects both PK and PD:
  - Example:
    - **Proteins** get degraded in the GI tract, so **oral is ineffective**, but **intramuscular works**.
    - **Morphine** has slower onset orally but **faster via IM**.
- **Therapeutic Window** is defined by:
  - **Absorption** rate
  - **Elimination/metabolism** speed

Examples:

Drug	Use	Dosing Frequency
Tetracycline	Infections	Every **6–8 hours**
Digoxin	Heart failure	Once **daily**
