

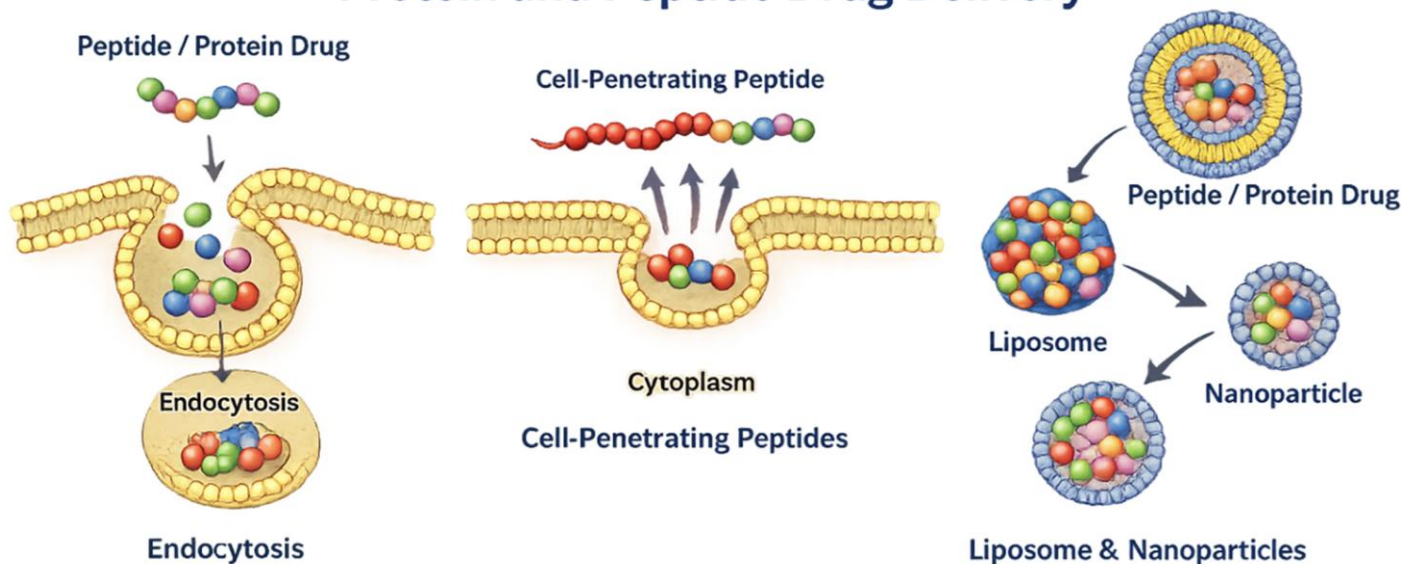
Protein and Peptide Delivery

Protein and Peptide Drug Delivery

Introduction

- Proteins and peptides are large biological molecules composed of chains of amino acids.

Protein and Peptide Drug Delivery



- They play important roles in the body as hormones, enzymes, antibodies, and structural components.
- These drugs are often referred to as biopharmaceuticals or biologics, and they differ significantly from conventional small-molecule drugs.
- Unlike small drug molecules, proteins and peptides are highly sensitive, unstable, and easily degraded in the body.
- Therefore, special drug delivery systems are required to protect them and ensure effective delivery.
- In modern medicine, proteins and peptides are widely used as therapeutic agents for the treatment of many diseases such as:
 - Diabetes
 - Cancer
 - Hormonal disorders
 - Immune disorders
 - Viral infections

Examples of Therapeutic Proteins and Peptides

- Insulin – used in diabetes treatment
- Growth hormone – used for growth disorders

- Monoclonal antibodies – used in cancer and autoimmune diseases
- Interferons – used for viral infections and cancer
- Vaccines

Main Goals of Protein and Peptide Drug Delivery Systems

- Stability
- Bioavailability
- Targeted delivery
- Therapeutic effectiveness

Characteristics of Proteins and Peptides

- Proteins and peptides have several unique physicochemical and biological properties that influence their drug delivery.
- **Important Characteristics:**
 - High molecular weight
 - Complex three-dimensional structure
 - Poor membrane permeability
 - Susceptibility to enzymatic degradation
 - Short biological half-life
 - High specificity and potency
 - Often water soluble
 - May trigger immune responses (immunogenicity)

Typical Properties of Proteins and Peptides

- **Property – Description**
 - **Molecular Weight** – Very large (1000 – >150,000 Da)
 - **Structure** – Complex three-dimensional structure
 - **Stability** – Easily degraded by heat, enzymes, and pH
 - **Solubility** – Often water soluble
 - **Immunogenicity** – May trigger immune responses

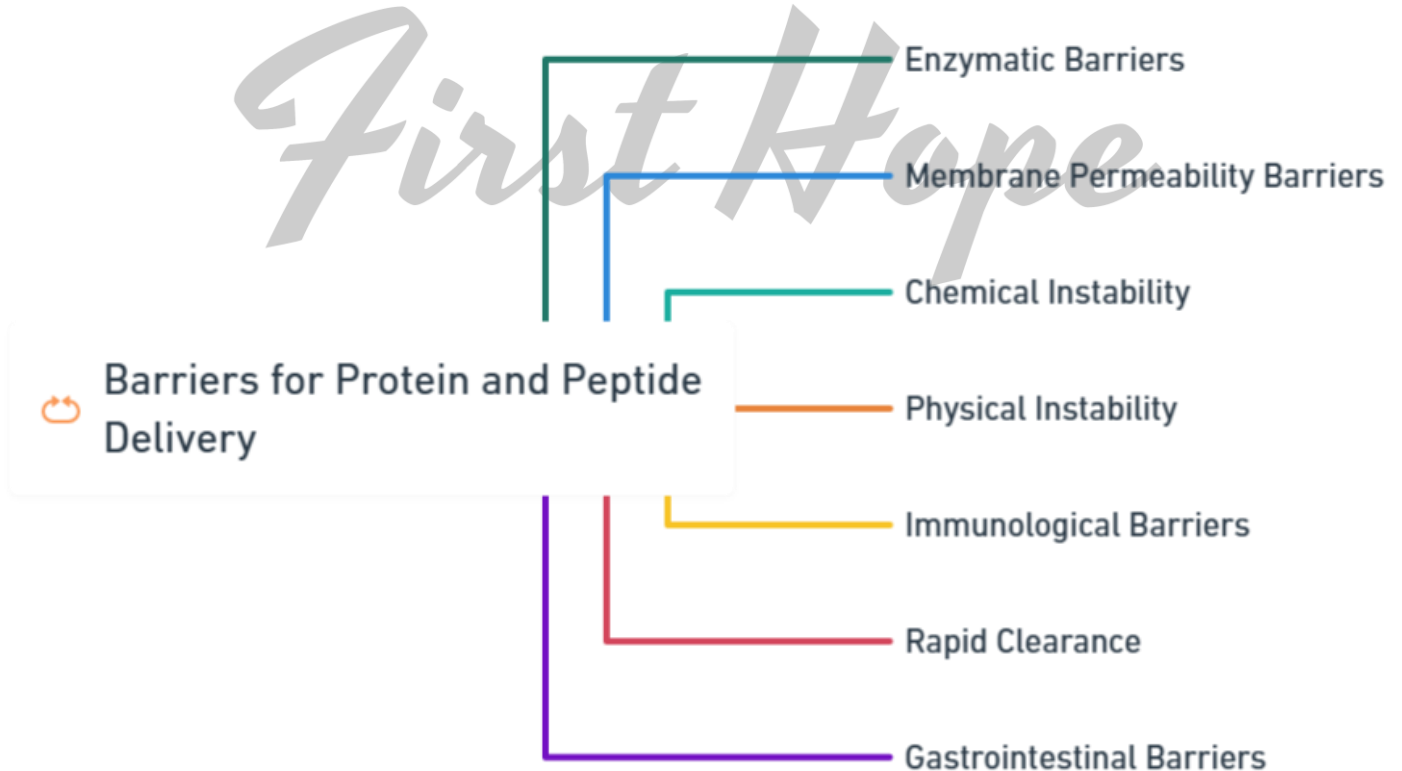
Challenges in Delivery

- Because of these properties, delivering proteins and peptides as drugs is difficult because:
 - They are easily degraded by enzymes in the body
 - They have poor permeability across biological membranes
 - They have short half-life in circulation

- Oral delivery is usually ineffective
- Therefore, special drug delivery approaches are required for their effective therapeutic use.

Barriers for Protein and Peptide Delivery

- Protein and peptide drugs face several biological barriers in the body that prevent them from reaching the target site effectively.
- **These barriers can be classified into:**
 - Enzymatic barriers
 - Membrane permeability barriers
 - Chemical instability
 - Physical instability
 - Immunological barriers
 - Rapid clearance
 - Gastrointestinal barriers (for oral delivery)



1. Enzymatic Degradation

- Proteins and peptides are easily broken down by enzymes called proteases and peptidases.
- **These enzymes are present in:**
 - Stomach – pepsin
 - Small intestine – trypsin, chymotrypsin

- Blood
- Cells
- When protein drugs are administered orally, digestive enzymes rapidly degrade them into amino acids before absorption.
- **Example:**
 - **Insulin** is destroyed in the stomach and intestine if taken orally.

2. Poor Membrane Permeability

- Biological membranes are mainly composed of lipid bilayers.
- Small lipophilic molecules pass easily through membranes.
- **However, proteins are:**
 - Large molecules
 - Hydrophilic
 - Often charged
- **Because of these properties, proteins cannot easily cross biological membranes such as:**
 - Intestinal epithelium
 - Skin barrier
 - Blood–brain barrier
- This results in low absorption and poor bioavailability.

3. Chemical Instability

- Proteins may undergo chemical degradation during formulation, storage, or in the body.
- **Common Chemical Degradation Reactions**

Oxidation

- Caused by oxygen or light
- Damages amino acids such as methionine and cysteine

Deamidation

- Conversion of amide groups in amino acids (asparagine and glutamine)
- Leads to structural changes

Hydrolysis

- Breakage of peptide bonds due to water
- These reactions reduce the biological activity of protein drugs.

4. Physical Instability

- Proteins possess complex three-dimensional structures.

- Changes in temperature, pH, or agitation can disturb this structure.
- **Major Types of Physical Instability**
 - Denaturation**
 - Loss of natural protein structure due to heat, pH changes, or chemicals
 - Aggregation**
 - Protein molecules stick together forming aggregates
 - Precipitation**
 - Proteins become insoluble and form precipitates
- These changes reduce the therapeutic effectiveness of protein drugs.

5. Immunogenicity

- Protein drugs may trigger immune responses because the body may recognize them as foreign substances.
- **This may lead to:**
 - Antibody formation
 - Allergic reactions
 - Reduced drug effectiveness
- Repeated administration increases the risk of immune reactions.

6. Rapid Clearance from the Body

- Protein drugs are often **rapidly removed from the bloodstream** by:
 - Kidney filtration
 - Enzymatic degradation
 - Uptake by liver and macrophages
- This results in a **short biological half-life**, requiring **frequent dosing**.

7. Gastrointestinal Barriers (For Oral Delivery)

- When proteins are administered **orally**, they encounter several barriers in the gastrointestinal tract.
- **Major GI Barriers**
 - Acidic stomach environment
 - Digestive enzymes
 - Poor intestinal absorption
- These factors lead to **very low oral bioavailability of protein drugs**.



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