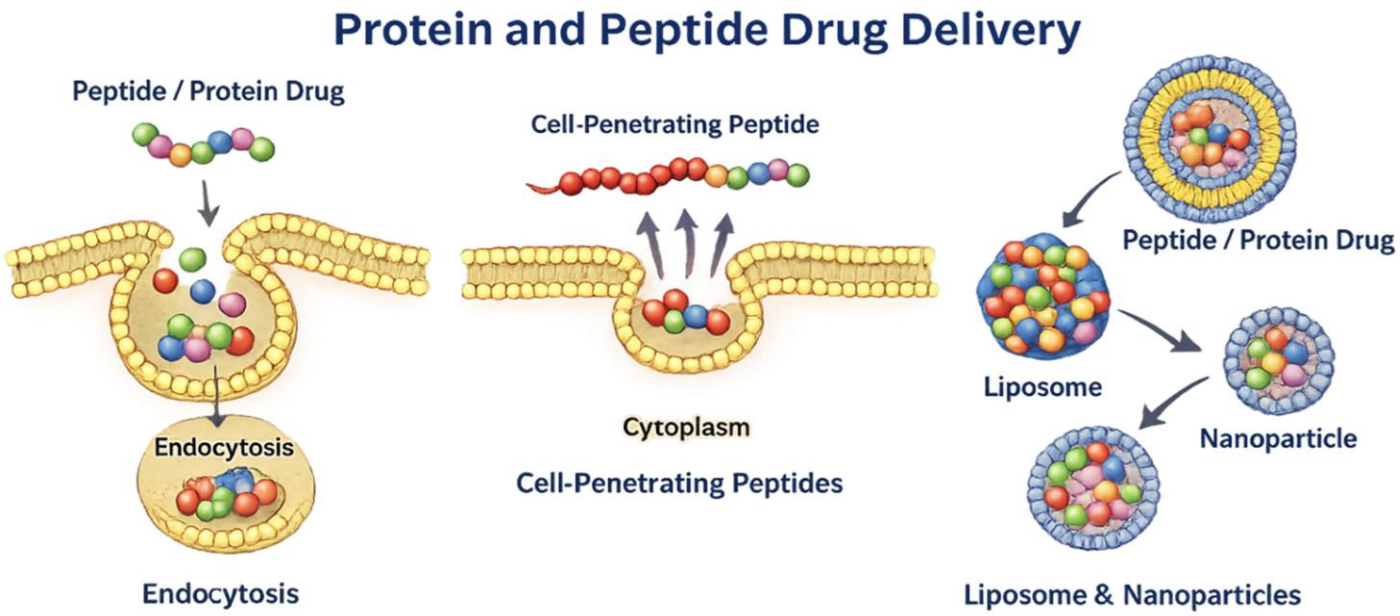
Protein and Peptide Delivery

Protein and Peptide Drug Delivery

Introduction

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



First Hope

- 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

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- 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)

First Hope

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

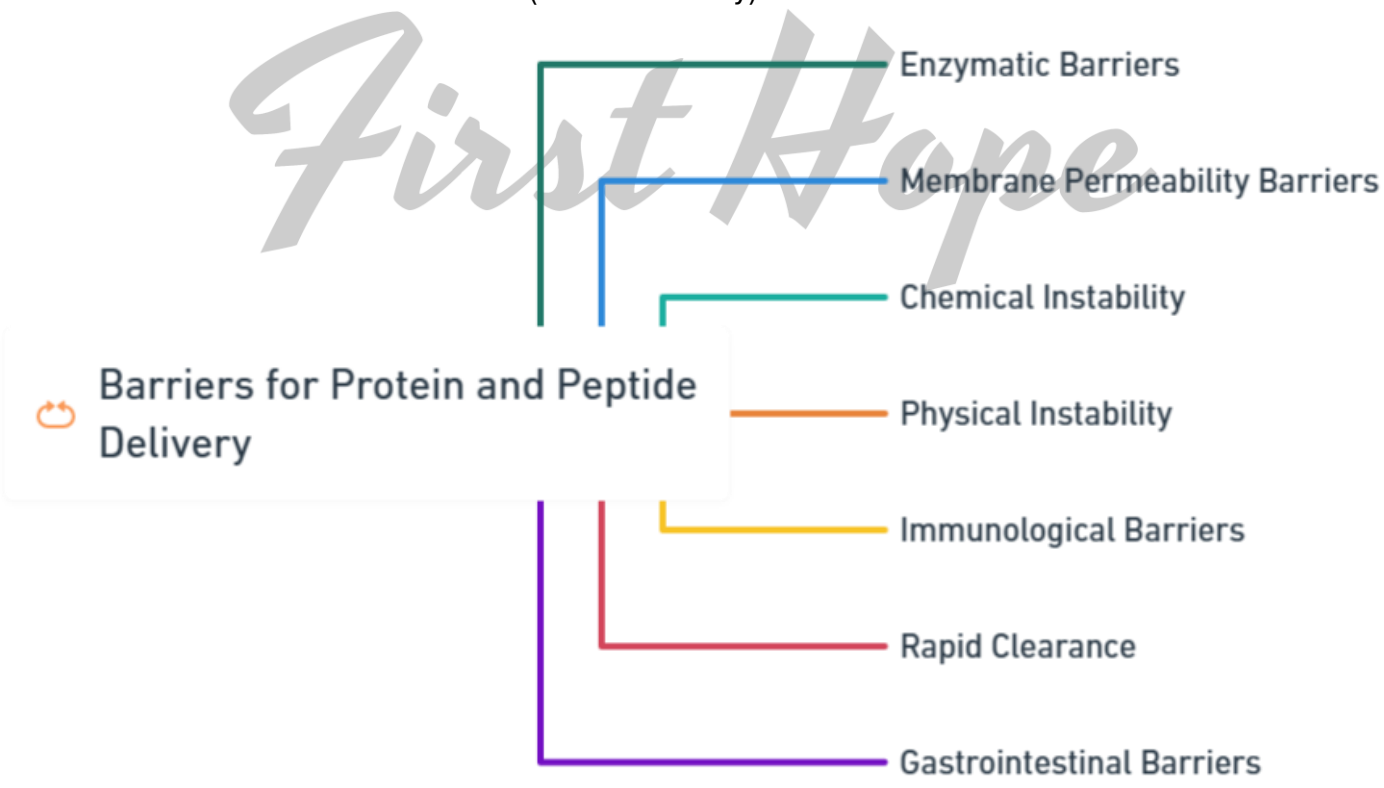
Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- 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

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- 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.

First Hope

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.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- 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**.

First Hope

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

First Hope

FREE PREVIEW

Click here to visit our website

PHARMACY PREMIUM NOTES

Complete subject and semesters are available on FirstHope app only.

Scan or click here

Click here to get the app >

Available on Google Play

JOIN THE FIRSTHOPE COMMUNITY

Join our Telegram channel

Click here to join Telegram >

Scan or click here

@FirstHopeNotes

Instagram

@firsthope.official

Click here to follow >

YouTube channel

FirstHope-Pharmacy / Live streams

Click here to watch >

WhatsApp channel

Follow FirstHope on WhatsApp

Click here to join >

FirstHope website

firsthope.co.in

Click here to visit >

B.Pharm / D.Pharm / M.Pharm / Pharm.D

Preview notes. Complete subjects and semesters in the FirstHope app.