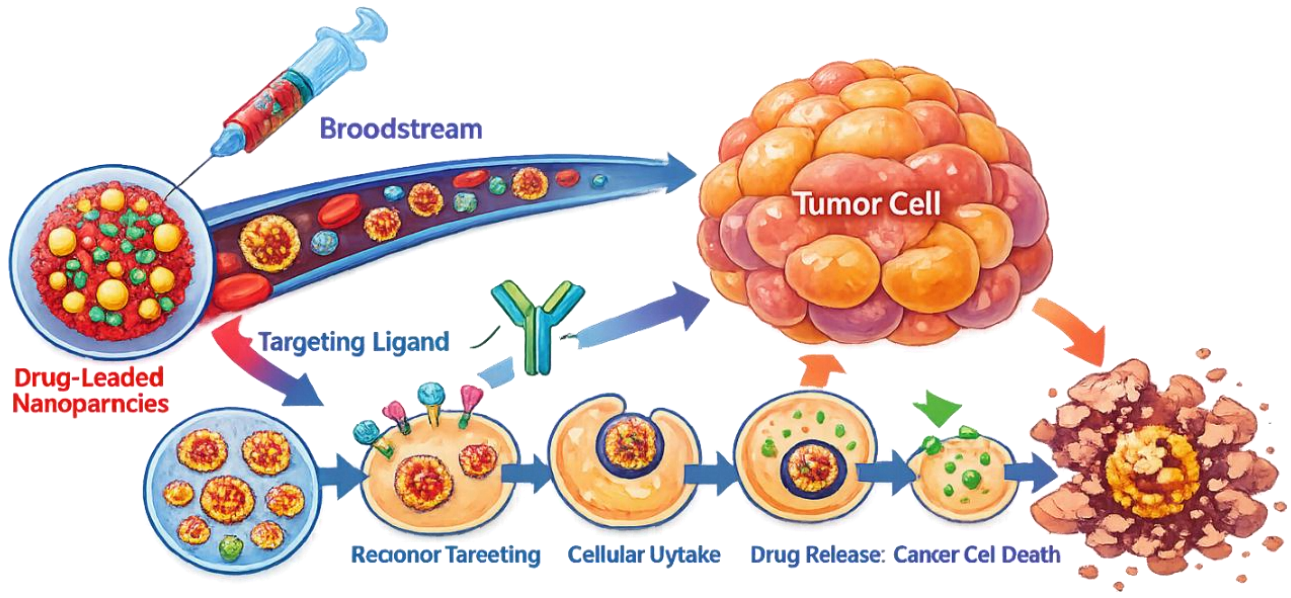
FirstHope Notes | B.Pharm Semester 7

Targeted Drug Delivery

Targeted Drug Delivery

- Targeted drug delivery enhances therapeutic efficacy by directing medications to specific cells or tissues, minimizing side effects compared to traditional systemic administration.



Key Concepts

1. **Selective Targeting:** Directing drugs specifically to disease sites (e.g., tumors, inflamed tissues).
2. **Controlled Release:** Sustaining drug release at the target site over time.
3. **Reduced Systemic Exposure:** Limiting drug interaction with non-target tissues to minimize adverse effects.

Approaches to Targeted Drug Delivery

1. **Passive Targeting:** Exploits physiological differences in diseased tissues (e.g., Enhanced Permeability and Retention (EPR) effect in tumors).
2. **Active Targeting:** Modifies drug carriers with ligands (e.g., antibodies, peptides) to bind specific receptors on target cells.
3. **Stimuli-Responsive Systems:** Activates drug release in response to local triggers like pH, temperature, or enzymes.
4. **Physical Targeting:** Uses external forces (e.g., magnetic fields, ultrasound) to guide drug carriers to specific sites.

Advantages of Targeted Drug Delivery

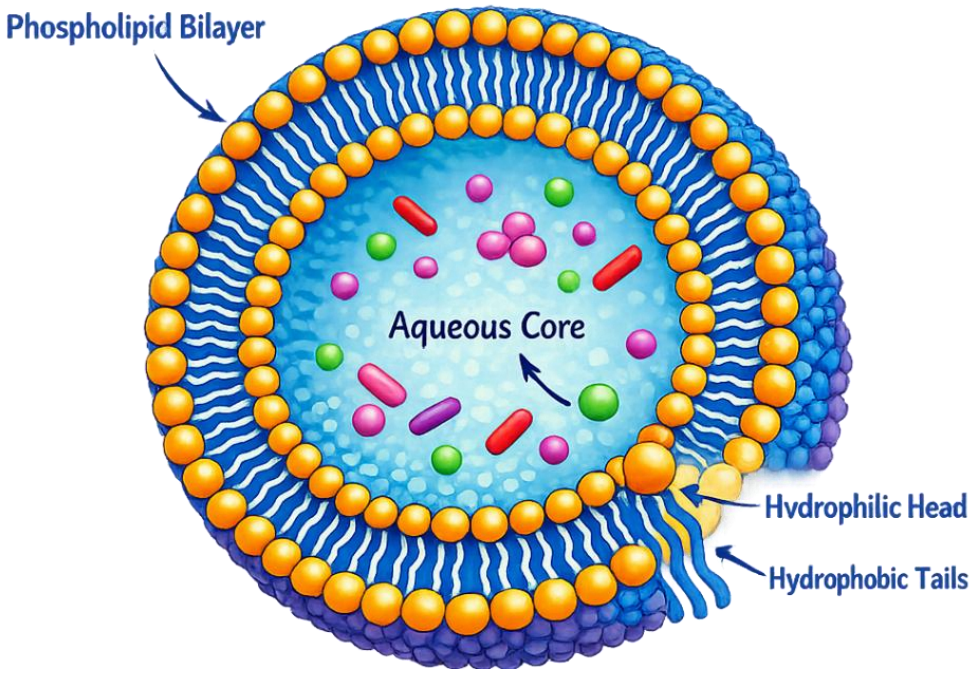
- **Increased Efficacy:** Higher drug concentrations at the target site enhances therapeutic outcomes.
- **Reduced Side Effects:** Minimizes drug exposure to non-target tissues, lowering adverse effects.
- **Improved Patient Compliance:** Enables lower dosages and less frequent administration.
- **Enhanced Stability:** Protects drugs from degradation before reaching the target.
- **Controlled Release:** Maintains therapeutic levels over extended periods.

Disadvantages of Targeted Drug Delivery

- **Complex Design:** Requires intricate engineering and biological insights.
- **High Cost:** Expensive production increases treatment costs.
- **Immunogenicity Risk:** Certain ligands or carriers may trigger immune responses.
- **Limited Penetration:** Challenges in reaching deep tissues or solid tumors.
- **Regulatory Barriers:** Novel systems face stringent approval processes.

Liposomes

- Liposomes are tiny spherical vesicles widely used as delivery systems for bioactive molecules.
- Formed by hydrating lipid molecules in an aqueous environment, they resemble cell membranes, making them biocompatible and suitable for interaction with human cells.

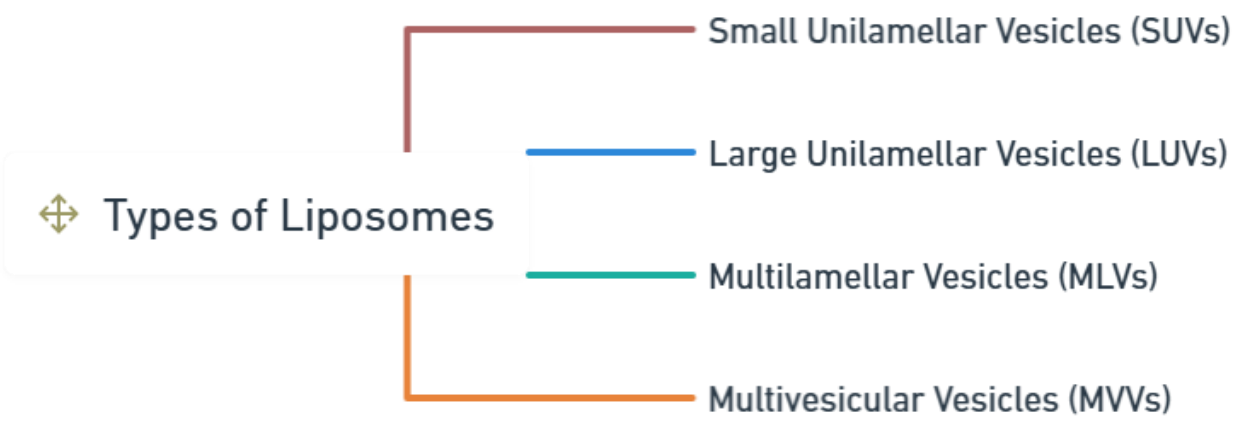


Structural Composition

- **Core and Bilayer:** An aqueous core surrounded by one or multiple concentric lipid bilayers.

- **Phospholipids:** Composed of amphiphilic phospholipids, with hydrophilic "heads" facing outward and hydrophobic "tails" inward.
- **Organization:** Bilayers naturally form due to the amphiphilic nature of phospholipids.

Types of Liposomes



1. **Small Unilamellar Vesicles (SUVs):** Single bilayer, 20–100 nm diameter.
2. **Large Unilamellar Vesicles (LUVs):** Single bilayer, 100–1000 nm diameter.
3. **Multilamellar Vesicles (MLVs):** Multiple concentric bilayers, 500 nm to micrometers.
4. **Multivesicular Vesicles (MVVs):** Large vesicles containing smaller vesicles.

Preparation Methods

1. **Thin Film Hydration:** Solvent evaporation forms a thin lipid film, hydrated with an aqueous solution.
2. **Sonication:** Ultrasonic waves reduce vesicle size.
3. **Extrusion:** Liposome suspension is passed through membranes to control size.

Applications

1. **Drug Delivery:** Encapsulates hydrophilic and lipophilic drugs, improving bioavailability and enabling targeted delivery.
2. **Vaccine Delivery:** Encapsulates antigens, enhancing immune response.
3. **Gene Therapy:** Transports genetic material for therapeutic applications.
4. **Cosmetics:** Enhances skin penetration and hydration in products.

Characterization

1. **Size & Lamellarity:** Range from nanosized to microsized, unilamellar or multilamellar.
2. **Surface Charge:** Cationic, anionic, or neutral based on lipid composition.
3. **Composition:** Phospholipid and cholesterol content.
4. **Drug Entrapment Efficiency:** Encapsulation capability.
5. **Release Profile:** Drug release mechanism and rate.

Advantages

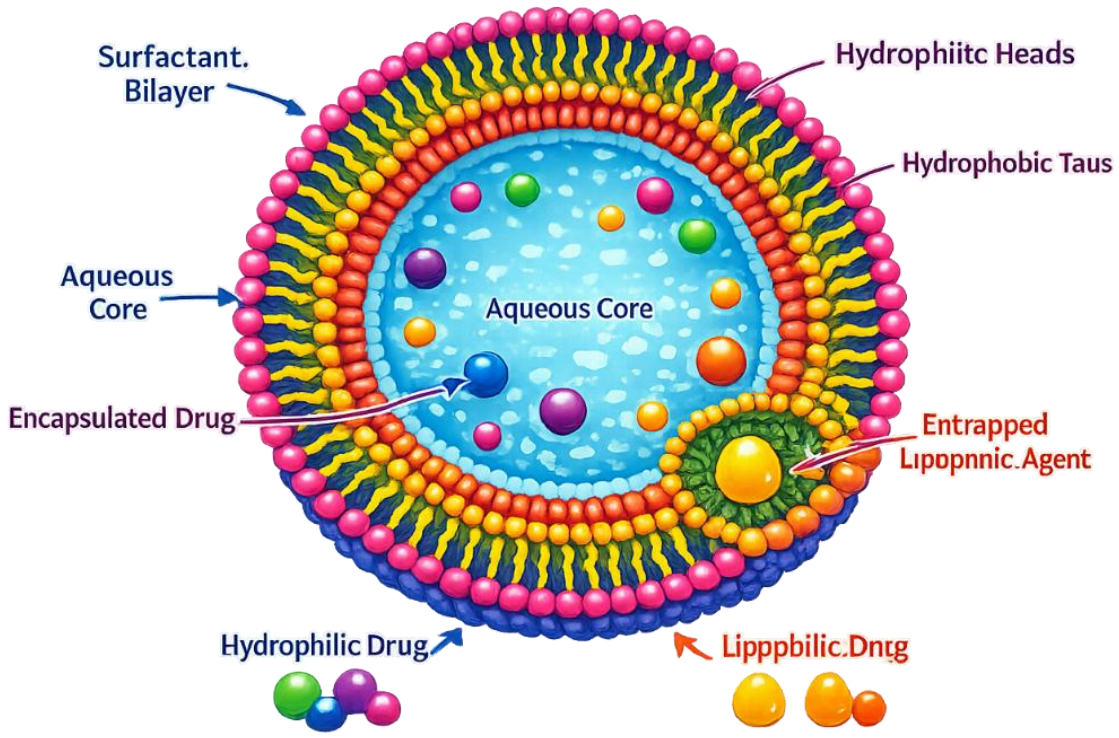
1. **Versatility:** Encapsulates hydrophilic and hydrophobic drugs.
2. **Biocompatibility:** Made of natural phospholipids, biocompatible and biodegradable.
3. **Protection:** Shields drugs from degradation.
4. **Prolonged Circulation:** PEGylation extends systemic circulation.
5. **Passive Targeting:** Exploits Enhanced Permeability and Retention (EPR) effect for tumors.
6. **Reduced Toxicity:** Limits drug exposure to non-target tissues.

Disadvantages

1. **Stability Issues:** Short shelf life and instability.
2. **High Cost:** Expensive production processes.
3. **Variable Drug Loading:** Inconsistent encapsulation efficiency.
4. **Leakage:** Drug may escape before reaching the target.
5. **Complex Production:** Requires specialized equipment.
6. **Clearance:** Susceptible to uptake by the reticuloendothelial system (RES).

Niosomes

- Niosomes are non-ionic surfactant vesicles with an aqueous core, similar in structure to liposomes but composed of synthetic non-ionic surfactants.
- This makes them more resistant to oxidative degradation compared to liposomes.



Structural Composition

- **Core and Bilayer:** An aqueous core surrounded by bilayers of non-ionic surfactants.
- **Surfactants:** Non-ionic surfactants with hydrophilic heads and hydrophobic tails, forming bilayers in water.
- **Cholesterol:** Incorporated to regulate membrane fluidity and stability.

Types of Niosomes

1. **Small Unilamellar Vesicles (SUVs):** Single bilayer, small-sized vesicles.
2. **Large Unilamellar Vesicles (LUVs):** Single bilayer, larger vesicles.
3. **Multilamellar Vesicles (MLVs):** Multiple concentric bilayers.

Preparation Methods

1. **Thin Film Hydration:** Forms a surfactant film by solvent evaporation, followed by hydration.
2. **Microfluidization:** Applies force to mix surfactant and aqueous phases, forming vesicles.
3. **Sonication:** Uses ultrasonic waves to generate niosomes from a surfactant mixture.

Applications

1. **Drug Delivery:** Encapsulates hydrophilic and lipophilic drugs, enabling controlled release, improved bioavailability, and targeted delivery.
2. **Dermatology:** Enhances transdermal drug absorption for improved skin penetration.
3. **Diagnostics:** Carries diagnostic agents for imaging and diagnostic procedures.
4. **Cosmetics:** Moisturizing and hydrating properties make them useful in skincare products.

Advantages

1. **Cost-Effective:** Made from cheaper synthetic surfactants.
2. **Enhanced Stability:** More stable than liposomes, resistant to oxidation and hydrolysis.
3. **Versatility:** Capable of encapsulating both hydrophilic and hydrophobic drugs.
4. **Improved Bioavailability:** Enhances dissolution and absorption of poorly soluble drugs.
5. **Controlled Release:** Offers sustained drug release over extended periods.
6. **Targeted Delivery:** Can be modified for active targeting to specific cells or tissues.
7. **Reduced Toxicity:** Minimizes systemic toxicity by localizing drug delivery.

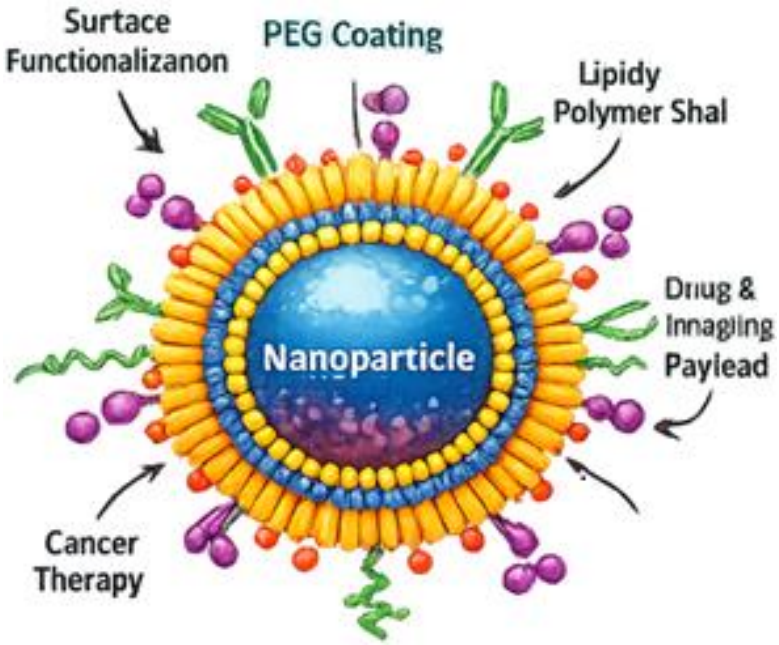
Disadvantages

1. **Leakage and Fusion:** Susceptible to drug leakage and vesicle fusion during storage.
2. **Variable Drug Entrapment:** Entrapment efficiency depends on preparation methods and drug properties.
3. **Scaling Challenges:** Large-scale production requires advanced methods and equipment.

4. **Storage Issues:** Requires specific storage conditions to prevent aggregation or leakage.
5. **Irritation Potential:** Some surfactants may irritate skin or mucous membranes, limiting use in certain applications.

Nanoparticles

- Nanoparticles are ultrafine particles ranging from 1 to 100 nm.
- In drug delivery systems (NDDS), nanoparticles are engineered to enhance therapeutic outcomes by facilitating targeted delivery, crossing biological barriers, and accessing hard-to-reach disease sites.



Preparation Methods

1. **Solvent Evaporation:** Drug and polymer are dissolved in an organic solvent, emulsified in water, and the solvent evaporates to form nanoparticles.
2. **Nano-precipitation:** Drug and polymer in a solvent are added to a non-solvent, inducing nanoparticle formation.
3. **Emulsion Polymerization:** Monomers polymerize in the presence of surfactants and stabilizers to create nanoparticles.
4. **High-Pressure Homogenization:** A liquid dispersion of drug and polymer is passed through a homogenizer to produce nanoparticles.

Advantages

1. **Improved Solubility:** Enhances the solubility of poorly water-soluble drugs.
2. **Targeted Delivery:** Directs drugs to specific tissues or cells, minimizing side effects.
3. **Controlled Release:** Sustains drug release over time, reducing dosing frequency.
4. **Protection:** Shields drugs from degradation in the body.

5. **Improved Bioavailability:** Increases the drug's active presence at the site of action.
6. **Multifunctionality:** Combines therapeutic and diagnostic agents for theranostics.

Disadvantages

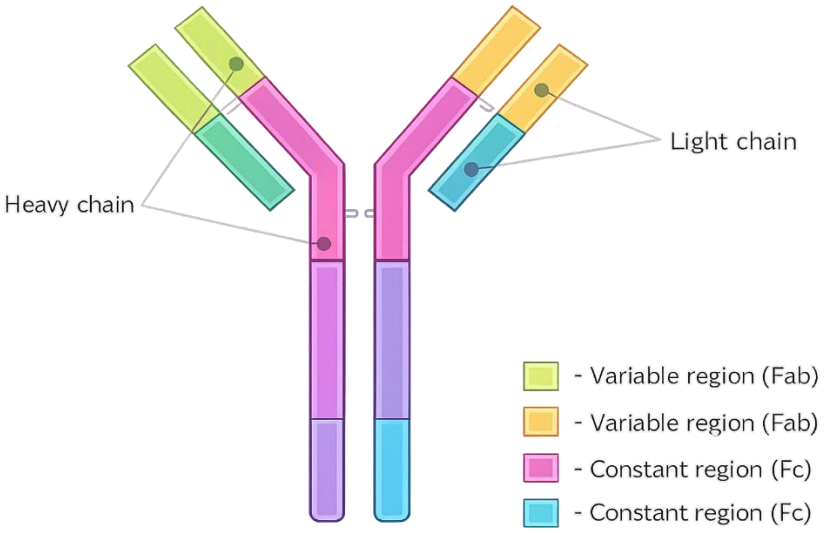
1. **Toxicity:** Potential issues with toxicity due to size or material composition.
2. **Manufacturing Scale-Up:** Challenges in scaling production for commercial use.
3. **Stability Issues:** Aggregation or degradation during storage can impact performance.
4. **Clearance by RES:** Rapid clearance by the immune system may reduce efficacy.
5. **Regulatory Challenges:** Complex approval processes can delay market introduction.
6. **High Cost:** Production and validation are expensive compared to traditional formulations.

Applications

1. **Targeted Drug Delivery:** Precisely directs drugs to diseased cells or tissues for maximum efficacy.
2. **Enhanced Solubility:** Improves the bioavailability of poorly soluble drugs.
3. **Controlled Release:** Provides sustained therapeutic drug levels over extended periods.
4. **Diagnostic Imaging:** Metallic nanoparticles serve as contrast agents for MRI, CT, and optical imaging.
5. **Combination Therapies:** Enables co-delivery of multiple agents for conditions like cancer.
6. **Gene Delivery:** Delivers genetic material to cells for treating genetic disorders or modulating gene expression.

Monoclonal Antibodies

- Monoclonal antibodies are laboratory-produced proteins that specifically bind to unique antigens on cells or proteins.
- Originating from a single B-cell clone, they exhibit identical specificity and binding affinity, making them a powerful tool in targeted therapies.



Production of Monoclonal Antibodies

1. Hybridoma Technology:

- Developed by Köhler and Milstein (1975), hybridoma technology combines B cells with myeloma cells to create hybridomas that produce mAbs.

Steps:

a) **Immunization:** Host animals (typically mice) are immunized with the target antigen.

b) **B Cell Isolation:** Spleen cells containing B lymphocytes are harvested.

c) **Cell Fusion:** B cells are fused with myeloma cells using agents like PEG.

d) **Selection:** Hybridomas are cultured in selective media (e.g., HAT medium) to ensure only fused cells survive.

e) **Screening:** Hybridomas producing the desired antibody are identified via assays (e.g., ELISA).

f) **Cloning:** Positive hybridomas are cloned to ensure monoclonality.

g) **Expansion & Production:** Clones are grown in culture or ascites for large-scale mAb production.

h) **Purification:** Antibodies are purified using protein A/G chromatography.

2. Advanced Methods:

1. Recombinant DNA Technology:

- **Steps:** Clone antibody genes from B cells, express in host cells (e.g., CHO cells).
- **Advantages:** Produces human or humanized antibodies, scalable.

2. Phage Display:

- **Steps:** Display antibody fragments on bacteriophages, select binders through panning.

- **Advantages:** No animal use, rapid, high-throughput, generates human antibodies.

3. **Transgenic Animals:**
   - **Method:** Use animals engineered with human antibody genes to produce fully human mAbs via hybridoma-like processes.
   - **Advantages:** Fully human antibodies with reduced immunogenicity.

Structure

- **Y-Shaped Protein:** Two heavy chains and two light chains.
- **Fab Region:** Binds to specific antigens with high affinity.
- **Fc Region:** Mediates interactions with the immune system.

Applications

1. **Cancer Therapies:** Targets tumor-specific antigens or delivers toxic agents to cancer cells.
2. **Autoimmune Diseases:** Blocks inflammatory molecules (e.g., TNF-alpha inhibitors for rheumatoid arthritis).
3. **Infectious Diseases:** Neutralizes pathogens or toxins.
4. **Organ Transplantation:** Suppresses immune response to prevent organ rejection.
5. **Cholesterol Management:** PCSK9 inhibitors reduce blood cholesterol levels.
6. **Diagnostics:** Detects specific proteins or molecules in disease diagnostics.

Advantages

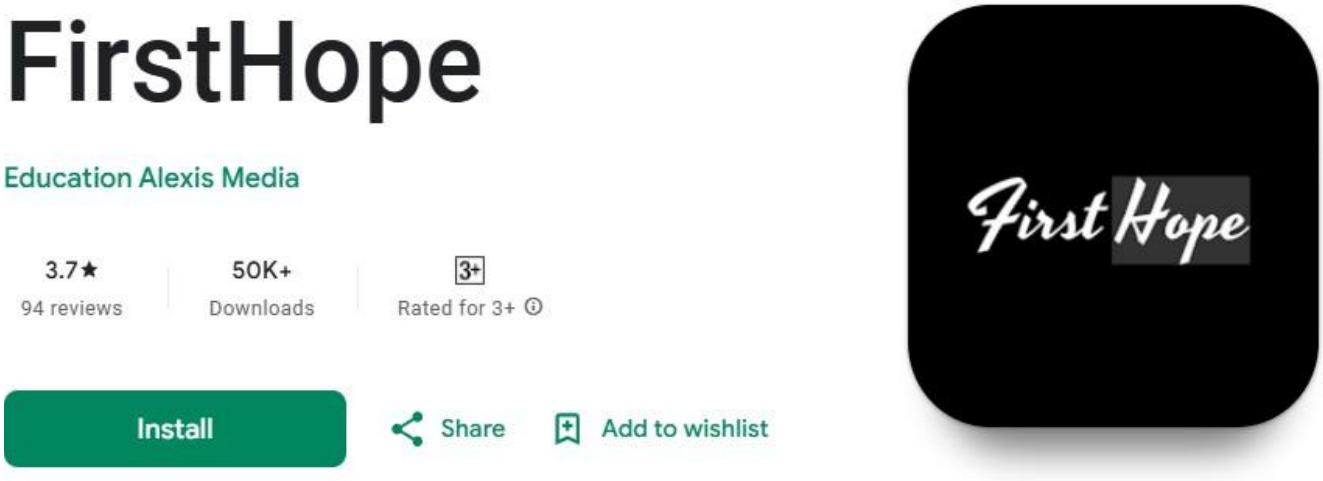
1. **High Specificity:** Targets diseased cells or molecules without harming healthy tissues.
2. **Reduced Side Effects:** Precise targeting minimizes off-target effects.
3. **Personalization:** Custom-designed for individual patients or conditions.
4. **Versatility:** Can be conjugated with drugs, toxins, or isotopes for multifunctional therapies.
5. **Known Mechanism:** Facilitates drug development and approval processes.

Disadvantages

1. **Cost:** Expensive development and production.
2. **Administration Challenges:** Often requires intravenous infusion.
3. **Immunogenicity:** Risk of immune reactions to non-humanized mAbs.
4. **Resistance:** Pathogens or tumors may develop resistance.
5. **Limited Penetration:** May struggle to infiltrate solid tumors.
6. **Stability Issues:** Sensitive to environmental factors like temperature and pH.

First Hope

Easy Short Notes Designed to Help You Score Better



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