

Targeted drug delivery: Innovations in pharmacoscience and biomedical applications.

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Introduction

The field of Targeted Drug Delivery has transformed modern therapeutics by enabling precise localization of pharmacological agents to diseased tissues or cells while minimizing systemic exposure. In phamas scine and biomedile, this approach leverages molecular targeting, carrier technologies, and controlled release systems to enhance therapeutic efficacy, reduce toxicity, and overcome biological barriers. Recent advances in nanotechnology, ligand-receptor engineering, and imaging-guided delivery have paved the way for next-generation therapies across oncology, infectious diseases, and regenerative medicine. Exploits physiological differences—such as enhanced permeability and retention (EPR) in tumor vasculature—to accumulate drug carriers preferentially in diseased areas. Lipid nanoparticles and polymeric micelles, by virtue of their nanoscale dimensions (typically 10–200 nm), extravasate through leaky capillaries and remain retained in tumor interstitium [1].

Involves the functionalization of drug carriers (e.g., nanoparticles, liposomes, dendrimers) with ligands—antibodies, peptides, or small molecules—that bind selectively to overexpressed receptors on target cells. Examples include folate-conjugated liposomes targeting folate receptor—positive ovarian cancer cells or RGD-peptide—modified nanoparticles binding integrins on angiogenic endothelium. These strategies often operate in tandem: a nanoparticle may rely on passive accumulation to reach tumor tissue, then employ an antibody fragment on its surface to engage tumor-specific antigens for cellular internalization [2].

Active targeting vectors bind specific cell-surface receptors (e.g., transferrin receptor, EGFR), triggering clathrin- or caveolin-mediated endocytosis. The carrier is then trafficked to endosomal compartments where pH-sensitive linkers or membrane-disruptive elements facilitate cargo release into the cytoplasm. Larger particles or opsonized carriers may be internalized via nonspecific pathways, especially in phagocytic cells like macrophages. While beneficial for targeting immune cells in inflammatory diseases, nonspecific uptake in off-target tissues can reduce overall specificity. Certain lipid nanocarriers can fuse directly with the plasma membrane, releasing their payload into the cytosol. This mechanism is often seen with cationic liposomes in gene delivery applications [3].

Nanoparticles co-loaded with paclitaxel and siRNA targeting BCL-2 have been designed to overcome chemoresistance. Surface conjugation with anti-EGFR antibodies directs these carriers to TNBC cells overexpressing EGFR, improving apoptosis induction while sparing healthy tissue. Crossing the blood–brain barrier (BBB) is a major challenge. Nanocarriers functionalized with transferrin or angiopep-2 peptides leverage receptor-mediated transcytosis to deliver temozolomide-loaded nanoparticles directly into glioma cells, enhancing intracranial drug exposure Inhalable lipid nanoparticles loaded with siRNA against KRAS have demonstrated reduced metastatic burden in murine models. Aerosolized delivery exploits pulmonary targeting to maximize local uptake while minimizing systemic toxicity [4].

Macrophage-targeted liposomes encapsulating rifampicin and isoniazid achieve high intracellular concentrations within Mycobacterium-infected cells. Mannose receptor-targeted liposomes enhance uptake by alveolar macrophages, leading to improved bactericidal activity and reduced dosing frequency. Polymeric nanoparticles bearing hepatitis B surface antigen (HBsAg) have been used to deliver nucleoside analogs directly to infected hepatocytes. Galactose-modified carriers preferentially bind the asialoglycoprotein receptor on hepatocytes, reducing off-target effects on renal and neuronal tissues [5].

Injectable hydrogels containing nanoparticles loaded with vascular endothelial growth factor (VEGF) target ischemic myocardium. The hydrogel depot ensures sustained release, promoting angiogenesis and reducing infarct size. Thermoresponsive nanoparticles carrying anti-inflammatory cytokines (e.g., interleukin-1 receptor antagonist) are injected intraarticularly. Cartilage-targeting peptides increase retention within the joint, alleviating inflammation and cartilage degradation [6].

By concentrating drugs at the pathological site, targeted delivery reduces the maximum tolerated dose (MTD) required to achieve efficacy, thereby minimizing systemic toxicity. Nanocarriers designed with stealth coatings (e.g., PEGylation) evade RES clearance, prolong circulation half-life, and penetrate dense tumor stroma or fibrotic tissues. Theranostic carriers incorporate imaging agents (e.g., fluorescent dyes, radionuclides) alongside therapeutic payloads, enabling simultaneous tracking of biodistribution and treatment response [7].

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Repeated administration of foreign nanomaterials may trigger complement activation or accelerate blood clearance (ABC) phenomena. Surface modification strategies (e.g., zwitterionic coatings) are under investigation to mitigate immune recognition. Tumor antigen heterogeneity can lead to subpopulations of cells that escape targeted therapy. Combination strategies—employing multiple ligands or bispecific antibodies—are being explored to address this issue [8].

Manufacturing uniform nanoparticles with narrow size distribution, consistent drug loading, and stable surface functionalization remains a technical and regulatory challenge for clinical translation. Comprehensive characterization of nanoformulations—covering physicochemical properties, sterility, endotoxin levels, and toxicity profiles—is required to satisfy regulatory guidelines. Long-term biodistribution and potential accumulation in off-target organs (e.g., liver, spleen) necessitate thorough preclinical toxicology studies.

Machine learning algorithms trained on large datasets of nanoparticle characteristics and in vivo outcomes can predict optimal carrier compositions for specific disease models. AI-guided simulations reduce empirical trial-and-error, accelerating the discovery of novel targeting ligands and delivery platforms. By coating polymeric cores with cancer cell or red blood cell membranes, researchers have created “invisibility cloaks” that evade immune clearance and exhibit homotypic targeting to tumor cells [9].

Harvested from mesenchymal stem cells or patient-derived cells, exosomes naturally carry endogenous cargo and can be engineered to deliver small molecules or nucleic acids. Early clinical trials are evaluating exosome-mediated siRNA delivery in pancreatic cancer. Targeted delivery of CRISPR–Cas9 components using lipid nanoparticles or viral vectors aims to correct genetic mutations in situ. In Duchenne muscular dystrophy models, muscle-homing peptides guide nanocarriers to skeletal muscle fibers, restoring dystrophin expression through localized genome editing.

Leveraging patient-specific biomarkers—such as tumor receptor profiling or immune cell signatures—will enable the customization of carrier design and ligand selection. Personalized nanoformulations promise higher response rates and reduced adverse events in heterogeneous populations. Regulatory Harmonization and Standardization:

International consortia are developing standardized protocols for nanoparticle characterization (size, zeta potential, endotoxin levels) and establishing consensus on safety endpoints. Streamlined regulatory pathways for Targeted Drug Delivery products will facilitate faster clinical adoption [10].

Conclusion

Targeted Drug Delivery represents a paradigm shift in pharma

science and biomedicine, offering precision therapeutics that align with the goals of personalized medicine. By engineering carrier systems ranging from polymeric nanoparticles to biomimetic exosomes and integrating molecular targeting strategies, researchers are overcoming long-standing barriers to drug efficacy and safety. While challenges in immunogenicity, manufacturing scale-up, and regulatory approval remain, advances in AI-driven design, biomimetic carriers, and gene editing delivery platforms will accelerate the translation of next-generation targeted therapies. As the field matures, collaboration between multidisciplinary teams spanning bioengineers, pharmacologists, clinicians, and regulatory experts will be essential to realize the full potential of targeted drug delivery in improving patient outcomes.

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