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Nanoparticles in Targeted Drug Delivery: Biochemical Mechanisms and Therapeutic Applications

Ume Salma[1*], Shazba Aziz[2], Abu Talib[3], Tasawar Iqbal[4], Nadeem Ahmed[4] and Sidra Altaf[5]

1. Department of Zoology, Wildlife and Fisheries, University of Agriculture Faisalabad, Pakistan
2. Department of Biochemistry, University of Agriculture Faisalabad, Pakistan
3. Department of Zoology, Government College University Faisalabad, Pakistan
4. Institute of Physiology and Pharmacology, University of Agriculture Faisalabad, Pakistan
5. Department of Pharmacy, University of Agriculture Faisalabad, Pakistan

*Corresponding Author: **janam5400@gmail.com**

ABSTRACT

Targeted drug delivery system development revolutionized modern therapeutics, with nanoparticles at the forefront as agents improving drug efficacy with minimal side effects. This review will examine the physicochemical properties of nanoparticles that allow their application in drug delivery, particularly regarding their ability to take advantage of the enhanced permeability and retention effect in diseased tissues. It throws light on different types of nanoparticles, namely liposomes, polymeric nanoparticles, and metal-based NPs for their efficacy in anticancer therapy, and treatment of neurodegenerative diseases and infections. Drug delivery mechanisms have been divided into passively and actively targeted drug delivery and reviewed cellular uptake pathways by which they attain precise localization. The toxicity and regulatory challenges affecting the clinical applications have also been discussed, which has given a lot of emphasis on the need for continuous research and innovation. This emphasizes the fields where nanomedicine may change treatment outlooks by providing more efficient and targeted therapies.

Keywords: Nanoparticles, drug delivery, mechanisms

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Introduction

Targeted drug delivery is one of the most significant innovations in modern therapeutics. It provides groundbreaking solutions to deliver drugs precisely to disease sites with minimized side effects. Nanoparticles (NPs) are very important in the transport of drugs due to their unique physicochemical properties: nanoscale size, high surface area, and surface modification ability. Nanoparticles (NPs) enhance drug accumulation at target sites, unlike conventional therapies. They exploit EPR in disease tissues and of course, different types of NPs emerge including liposomes, polymeric NPs, metal NPs, and carbon-based NPs. Active targeting further enhances the accuracy of drug delivery wherein ligands attached on NP surfaces bind precisely to the receptors overexpressed on diseased cells improving therapeutic outcomes and reducing side effects. Researchers are working on stimuli-responsive nanocarriers to create even more efficient, targeted therapies that react autonomously to the microenvironment at the site of interest, in response to biological triggers such as pH fluctuations, enzymes, or temperatures. This review discusses nanoparticle-based drug delivery mechanisms, therapeutic applications and future challenges in the clinical translation of promising nanomedicine focusing on cancer, neurological disorders and antimicrobial therapies (1).

Biochemical Mechanisms of Targeted Drug Delivery

Nanoparticle-targeted drug delivery relies on advanced biochemical methods, including passive, active and cellular uptake pathways to optimize therapeutic precision and efficacy with minimal adverse effects.

Targeting Mechanisms

Passive Targeting. utilizes the EPR effect, which allows nanoparticles to be selectively accumulated in tumor tissues through abnormal leakiness of blood vessel walls. Ten to one hundred nanoparticles might penetrate and reside within the tumor microenvironment longer than they would otherwise in normal cells. However, based on tumor heterogeneity, among other variables, and the physicochemical characteristics of the nanoparticles, this may or may not be highly effective. Active Targeting involves changing the nanoparticle surface with specific ligands that bind to overexpressed receptors present on target cells. This targeted interaction improves drug delivery specificity by limiting exposure to healthy tissues and enabling greater concentrations of therapeutic drugs at the illness site. For example, folic acid functionalized nanoparticles can target cancer cells expressing folate receptors specifically, offering a more precise delivery method. Figure number one shows the Nanoparticles in the Targeted Drug Delivery (2).

Cellular Uptake Pathways

Nanoparticles enter cells through endocytosis, caveolin-mediated or clathrin-mediated, depending on size. The main process by which cells absorb nanoparticles is endocytosis. Receptor mediated uptake ensures selective internalization increasing delivery precision. Transcytosis enables drug delivery to difficult therapeutic sites by passing cellular barriers like the blood-brain barrier.

Controlled Release Systems

Regulating the release of therapeutic substances is an essential component of targeted drug delivery. Stimuli-responsive nanoparticles are designed to release their therapeutic payloads in response to specific cues in the sick tissues, including pH, enzyme activity, or temperature variations. For instance, pH-responsive nanoparticles minimize the damage on healthy cells by releasing drugs at acidic pH conditions associated with tumors, while they are stable at normal pH. Though the thermo-responsive release allows the drugs to be released in response to high temperatures associated with the tumor sites, the enzyme-triggered release utilizes the overactive enzymes found in tumors to facilitate the site-specific delivery (3).

Nanoparticle Types and Functionalization

There exist numerous forms of nanoparticles, each with different properties that make them more applicable in drug delivery. Metal and metal-oxide nanoparticles are also significant in targeted medication administration, which is important in imaging and treatment. For instance, gold nanoparticles are increasingly applied in photothermal therapy, targeting the killing of cancer cells by light consumption and subsequent generation of heat. They are suitable for targeted administration and diagnostics since they may be functionalized with a range of ligands. Using an external magnetic field, metal-oxide nanoparticles such as iron oxide can help in targeted therapy and are applicable in MRI. Additionally, carbon-based nanoparticles and quantum dots are soon to be utilized as diagnostic instruments because of their size tunable fluorescence, quantum dots have special optical characteristics that make them ideal for bioimaging and monitoring biological activities. Carbon based nanoparticles such as graphene and carbon nanotubes also possess remarkable electrical and thermal conductivity which may find use in biosensing particularly on identifying disease markers and medication administration. Table number one shows the information about nanoparticles in targeted drug delivery (4).

Mechanism of Action: Biochemical Pathways

Nanoparticles accumulate passively through leaky vasculature and poor lymphatic drainage in tumor tissues and inflammatory sites and are known as the enhanced permeability and retention (EPR) effect. They bypass normal tissues by exploiting enhanced vascular permeability, targeting diseased tissues with reduced clearance. Functionalization with ligands such as antibodies, peptides, or aptamers helps nanoparticles selectively bind to overexpressed receptors on target cells, such as cancer or inflammatory cells. For example, nanoparticles conjugated with Herceptin

are designed to target HER2 receptors in breast cancer. Once nanoparticles bind, they are internalized into the cells by pathways of endocytosis, such as clathrin-mediated, caveolae-mediated, or macropinocytosis. The therapeutic cargo is released intracellularly by pH-sensitive, enzyme-sensitive, or redox-sensitive mechanisms. Nanoparticles facilitate controlled release at the targeted site. pH-responsive systems exploit acidic tumor microenvironments. Enzyme-responsive systems depend on enzymes such as matrix metalloproteinases. Thermoresponsive systems depend on external heat stimuli. Nanoparticles are coated with polyethylene glycol (PEG) or similar hydrophilic polymers to evade immune recognition and prolong circulation. PEGylation minimizes opsonization by serum proteins, reducing clearance by macrophages. Therapeutically, nanoparticles deliver chemotherapeutic drugs directly to tumors, minimizing systemic toxicity. Doxorubicin-loaded liposomes (Doxil) effectively target cancer cells, promoting ROS generation and apoptosis. Methotrexate-conjugated gold particles in nanoparticles inhibit pro-inflammatory cytokines such as TNF-α, IL-6, and oxidative stress toward inflamed joints in the treatment of rheumatoid arthritis. Lipid-based nanoparticles support neurodegenerative drugs such as dopamine analogs for transportation across the blood-brain barrier (BBB) by receptor-mediated transcytosis. Antimicrobial nanoparticles prevent the action of resistant microbes by the disruption of microbial biofilms or cell walls with examples that include silver nanoparticles creating oxidative stress and prohibiting the activities of microbial enzymes. Nanoparticles improve diabetes management. Chitosan-based particles protect oral insulin from degradation and enhance gut absorption via mucoadhesion as well as by receptor-mediated uptake (5).

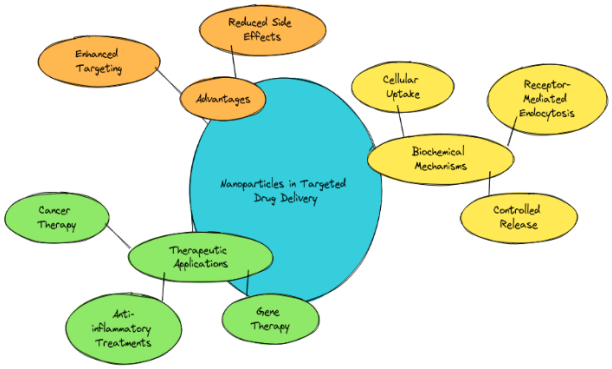

Fig. 1: Nanoparticles in the Targeted Drug Delivery

Therapeutic Applications

Cancer Therapy

Nanoparticles, in cancer therapy, have ensured targeted drug delivery directly to the cancer cells, sparing healthy tissue of the toxic ramifications of chemotherapy. Liposomes, polymeric nanoparticles, gold nanoparticles, and quantum dots are examples of these NPs, which have high specificity in delivering medications, genetic material, or immunotherapeutic agents to malignancy cells. Their distinct surface alterations enable various applications, including focusing on certain cancer cell receptors. NPs offer the possibility of a substitute for traditional treatments of cancer by enhancing precision and reducing side effects (6).

Neurological Disorders

Nanoparticles for the treatment of neurological disorders should be capable of passing the blood-brain barrier, which is a significant problem in the delivery of drugs to brain diseases. For such polymeric as well as lipid-based nanoparticles, this is particularly true. Drugs for diseases like neuro-degenerative diseases may now be transmitted directly to the brain and have less impact upon other parts of the body due to the passage of these nanoparticles through the blood brain barrier. This focused approach is a useful tactic for neurological therapy since it increases therapeutic efficacy and decreases negative side effects.

Microbial Infection

It has been increasingly recognized that in overcoming microbial infection, nanoparticles play a crucial role in dealing with drug resistance through the penetration of bacterial biofilm layers to directly kill bacterial cells because of their antibacterial qualities that effectively break down bacterial cell membranes and biofilm barriers. Silver and metal oxide NPs are often used when it comes to infections where conventional antibiotics are less effective. This type of NPs provides an excellent defense against multidrug-resistant (MDR) bacteria, which accelerates healing (7).

Future Directions and Challenges

The successful application of nanoparticles (NPs) in medicine faces several challenges that must be surmounted for safe and effective treatments. Key issues are with toxicity and biocompatibility as some nanoparticles specifically build up in tissues over time and potentially cause long term health effects, toxicity and biocompatibility. One important area of research directed towards reducing toxicity is the development of biodegradable NPs that can naturally decompose inside the body. Besides, nanoparticle-based treatments face complex regulatory requirements that may restrict clinical trials and approval procedures, regulatory and clinical translation continue to be major challenges. To advance these treatments to wider clinical use, these criteria will have to be harmonized globally, and frameworks tailored to nanomedicine should be developed (8, 9).

Table 1: The information about nanoparticles in targeted drug delivery

Sr. No.	Type of Nanoparticle	Biochemical Mechanism	Therapeutic Applications	Advantages
1	Liposomes	Encapsulation and controlled release of drugs	Cancer therapy	Biocompatibility, reduced toxicity
2	Dendrimers	Multivalent surface functionality	Gene delivery, cancer therapy	High loading capacity, precise targeting
3	Polymer-based NPs	Passive and active targeting	Rheumatoid arthritis, drug-resistant cancers	Controlled release, tunable properties
4	Metallic NPs	Photothermal and photodynamic mechanisms	Antimicrobial, cancer therapy	High stability, ease of surface modification
5	Quantum dots	Fluorescent imaging for drug delivery	Bioimaging, cancer diagnostics	Dual imaging and therapeutic potential
6	Carbon nanotubes	Drug absorption via pi-stacking interactions	Targeted delivery for CNS disorders	High surface area, enhanced permeability
7	Silica-based NPs	Mesoporous structures for drug loading	Anticancer, gene delivery	High drug loading, versatile functionalization
8	Polymeric micelles	Solubilization of hydrophobic drugs	Chemotherapy, cardiovascular diseases	Increased solubility, selective delivery
9	Protein-based NPs	Enzyme-responsive release	Diabetes, cardiovascular disorders	Biodegradability, minimal immunogenicity
10	Exosome-based NPs	Mimicking natural extracellular vesicles	Neurological disorders, cancer therapy	Biocompatibility, natural targeting ability

Conclusion

Nanoparticles are of considerable importance as they are poised to revolutionize modern medicine with novel approaches to targeted medication delivery, increasing therapeutic efficacy and decreasing adverse effects. The applicability and importance of nanoparticles are depicted through their use in antimicrobial therapies, neurological illnesses, and cancer therapy. Even though much work remains to be done in sorting out issues like toxicity and regulatory complexity, nanoparticle technologies are still under research to make safety profiles and therapeutic efficacy better. Due to the extensive application of nanoparticles in therapy, nanomedicine can potentially revolutionize the world of healthcare in the future.

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