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"Smart Nanocarriers For Cancer Treatment: A Comprehensive Insight Into Targeting Strategies And Stimuli-Responsive Drug Delivery Systems"

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Abstract

Cancer remains one of the leading causes of mortality worldwide, and the limitations of conventional therapies including poor drug selectivity, systemic toxicity, and multidrug resistance have accelerated the shift toward advanced nanotechnology-based treatment strategies. Nanomedicine offers remarkable potential to overcome these challenges through the development of smart nanocarriers capable of targeted delivery, improved tumour accumulation, and controlled drug release. This review provides a comprehensive overview of tumour-targeting mechanisms, including passive targeting via the Enhanced Permeability and Retention (EPR) effect and active targeting mediated by ligands such as antibodies, peptides, aptamers, and small molecules. Various nanocarriers including liposomes, dendrimers, polymeric micelles, carbon nanotubes, and gold nanoparticles are examined with respect to their structural features, advantages, and therapeutic applications in cancer treatment. Additionally, the role of endogenous and exogenous stimuli (pH, redox conditions, enzymes, temperature, light, and magnetic fields) in designing smart, stimuli-responsive drug delivery systems is discussed. Beyond therapeutic advances, this review highlights the economic and commercialization challenges faced by nanomedicine, including high production costs and limited large-scale industrial support, while emphasizing the long-term cost-effectiveness and clinical value of nanotherapeutics. Emerging approaches such as DNA-based nanostructures, hybrid nanoparticles, and next-generation cancer immunotherapies including nanoparticle-enabled cancer vaccines underscore the future direction of personalized oncology. Overall, nanotechnology continues to redefine cancer therapy by offering more precise, efficient, and patient-specific treatment options with the potential to greatly improve therapeutic outcomes.

Keywords: Nanomedicine, Targeted drug delivery, Stimuli-responsive nanocarriers, Gold nanoparticles, Aptamer-based targeting, etc.

1. Introduction

Cancer is a major global health concern, with both its incidence and mortality rising rapidly and causing nearly 10 million deaths every year. Chemotherapy remains one of the most widely used and effective treatment options. However, its therapeutic success is often limited because the drugs cannot distinguish well between healthy and cancerous cells. This lack of selectivity, combined with poor drug accumulation at the tumor site, reduces treatment effectiveness. Additionally, multidrug resistance, variations in the tumor microenvironment, and differences between individual patients further complicate efforts to achieve successful cancer therapy. These challenges have encouraged the search for more advanced and efficient drug delivery strategies.

At the molecular level, cancer typically arises from damage or mutations in proto-oncogenes, which normally promote controlled cell growth, and tumor suppressor genes, which help regulate cell division and trigger cell death when necessary. Mutations that favor unchecked cell growth, inhibit natural growth-control mechanisms, weaken the immune system's surveillance, prevent normal cell death, and allow genetic defects to accumulate all contribute to tumor development. While surgery and radiotherapy are effective for treating localized or non-metastatic cancers, they offer limited benefits once cancer cells spread to distant parts of the body.

Nanotechnology has emerged as a promising solution to these limitations. Nanoparticles, typically ranging from 10 to 100 nm, have a large surface area and excellent mobility within the body, allowing them to reach and penetrate targeted tissues more effectively. Their small size smaller than blood cells and comparable to DNA gives them unique physical, chemical, and optical properties that make them highly suitable for medical applications, especially in cancer diagnosis and therapy. Nanoparticles can be combined with drug molecules to create targeted delivery systems that direct treatment specifically to diseased tissues, improving therapeutic outcomes while reducing side effects. Along with enabling new treatment approaches, nanotechnology also enhances the performance of existing cancer therapies. (refer fig 1)

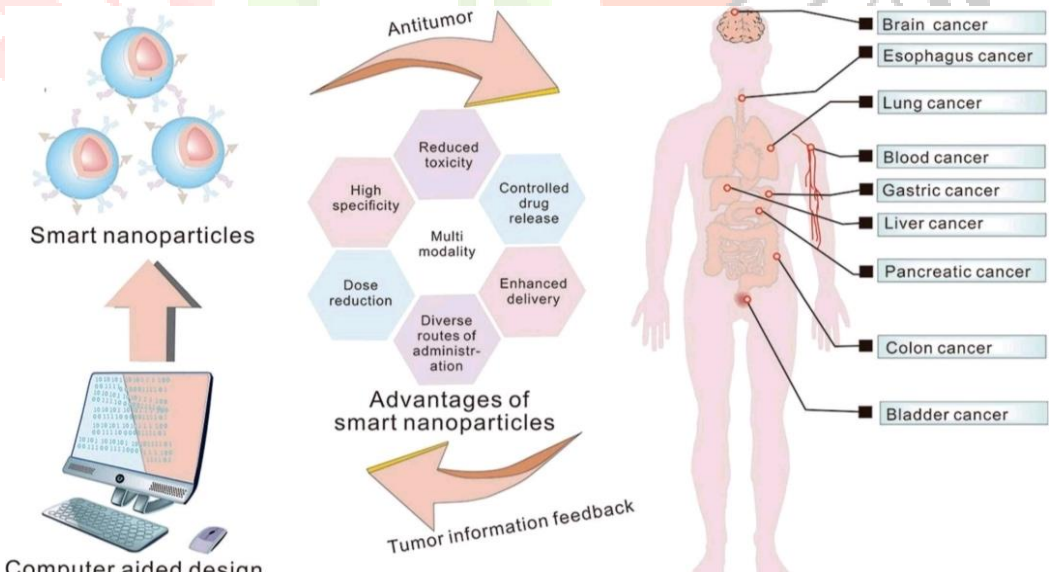


Fig. 1 - Schematic Illustration of Smart Nanoparticles for Cancer Treatment.

2. Drug Targeting

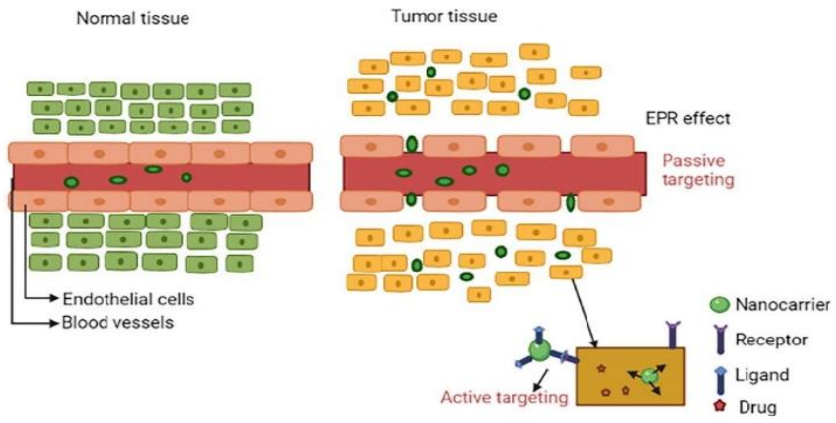
Smart nanocarriers designed for tumour targeting offer several advantages, including improved drug release, better internalization by cancer cells, enhanced pharmacokinetic and pharmacodynamic profiles, and higher delivery specificity. Most importantly, they help reduce toxic side effects. Tumours typically have leaky blood vessels and poor lymphatic drainage, making them suitable targets for specialized drug-delivery systems. Drug targeting approaches are generally categorized into passive targeting and active targeting.

2.1 Passive Targeting

Passive targeting relies mainly on the Enhanced Permeability and Retention (EPR) effect, a hallmark of tumour tissues. Tumour blood vessels are structurally abnormal and have large gaps in their endothelial lining. This allows drug-loaded nanoparticles to enter tumour tissues more easily than normal tissues this is the enhanced permeability aspect. Additionally, tumours often lack efficient lymphatic drainage, causing nanoparticles to remain inside the tumour for longer periods, which represents the enhanced retention effect. Together, these phenomena make up the EPR effect. The effectiveness of passive targeting depends on several factors, such as tumour vascular permeability, nanoparticle size, surface properties, and circulation time in the bloodstream. When compared to healthy tissues, passive targeting can increase drug specificity by 20–30%. Nanocarriers that can evade immune detection and circulate for extended periods show the best EPR-based accumulation. Within 1–2 days, drug-loaded smart nanocarriers can reach concentrations inside tumours that are 10–50 times higher than those in normal tissues.

2.2 Active Targeting

Active targeting uses surface-modified nanoparticles that can directly recognize and bind to specific molecules overexpressed on cancer cells. Many tumours exhibit elevated levels of surface markers such as folate receptors, transferrin receptors, various antigens, or other biomolecules. By attaching ligands like antibodies, peptides, folic acid, aptamers, or transferrin to nanocarriers, these systems can selectively bind to cancer cells and trigger receptor-mediated uptake. A classic example is immunoliposomes, which are liposomes conjugated with tumour-specific antibodies. These systems combine the drug-carrying capacity of liposomes with the precision of antibody targeting. For instance, doxorubicin-loaded immunoliposomes targeting the HER2 receptor have demonstrated significantly improved therapeutic outcomes against various breast cancers compared to standard PEGylated



liposomes. (refer fig 2)

Fig. 2 - Schematic Representation of Drug Targeting via Passive Targeting (EPR effect) Mode and Active Targeting Mode.

3. Nanocarriers used in Cancer Therapy

Nanoparticles have gained tremendous attention in cancer treatment because of their ability to carry drugs, enhance imaging, and deliver controlled drug release. They can encapsulate poorly water-soluble compounds and can be coated with hydrophilic materials or surfactants to ensure proper dispersion in biological fluids. Nanocarriers help protect drugs from degradation, prolong their circulation time, reduce renal clearance, improve the performance of cytotoxic agents, regulate drug-release patterns, and increase the solubility of many chemotherapeutic substances. Below are some of the most advanced and widely studied smart nanocarriers.

3.1 Liposomes

Liposomes are spherical vesicles composed of phospholipid bilayers enclosing a water-filled core. Their unique structure enables them to carry both hydrophilic and lipophilic drugs, making them one of the most versatile and widely researched drug-delivery systems.

Advantages of Liposomes include:

- High biocompatibility and low immunogenicity
- Ability to protect sensitive drugs
- Structural resemblance to cell membranes
- Good safety profile and prolonged circulation time

However, conventional liposomes also have limitations such as low drug-loading efficiency for some molecules, leakage of encapsulated hydrophilic drugs, and rapid clearance by the reticuloendothelial system (RES). When liposomes are identified as foreign particles, they are taken up by macrophages of the mononuclear phagocyte system (MPS), reducing their effectiveness. To overcome this, PEGylated liposomes were developed. The addition of a polyethylene glycol (PEG) coating reduces immune recognition and enhances stability in the bloodstream. Furthermore, the development of targeted liposomes engineered with ligands such as folate, mannose, peptides, transferrin, and antibodies allows for selective delivery to tumour cells. Recent advances include stimuli-responsive liposomes that release their drug payload only under specific tumour conditions such as acidic pH, hypoxia, or slightly elevated temperatures. For instance, pH-sensitive liposomes remain stable at physiological pH (~7.4), but break down at the mildly acidic tumour environment (~5.7), releasing the drug precisely where it is needed. Hyaluronic-acid-decorated pH-responsive liposomes have shown enhanced effectiveness against CD44- verexpressing cancer cells while reducing toxicity to normal tissues. Figure 3.1 provides a schematic representation of different liposomal types.

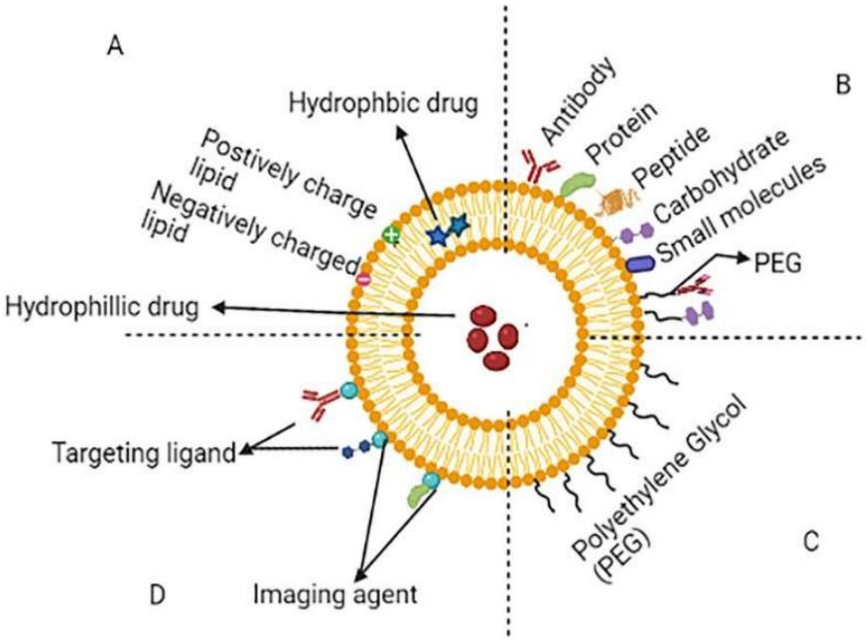


Fig. 3.1 - Schematic Representation of Different types of Liposomes. (A) Conventional Liposome (B) Ligand Targeted Liposome, (C) PEGylated Liposome (D) Theranostic Liposome.

Sr .no	Product Name	Type	Drug	Uses
1.	Vyxeos	Liposome	Daunorubicin and Cytarabine	Acute myeloid and leukamia.
2.	Doxil	PEGylated liposome	Doxorubicin	Ovarian and breast cancer
3.	Lipo dox	PEGylated liposome	Doxorubicin	Multiple myeloma ovarian and breast cancer
4.	Onivyde	PEGylated liposome	Irinotecan	Metastatic pancreatic cancer
5.	Marqibo	Liposome	Vincristine sulphate	Acute lymphoblastic leukemia

Table 1 - lists FDA Approved Liposomal Formulations used in Cancer Therapy.

3.2 Dendrimers

Dendrimers, also known as dendrons, take their name from the Greek word meaning *"tree,"* due to their highly branched, tree-like architecture. Structurally, dendrimers consist of three key components:

1. A central core, which serves as the foundation from which the branches grow.
2. Repeated branching units, arranged in layers called generations that expand outward in a radially symmetric manner.

3. Peripheral functional groups, located on the outer surface, which determine the dendrimer's pharmacokinetic behaviour and biocompatibility.

Although dendrimers offer excellent potential for drug delivery, cationic dendrimers can cause cell membrane damage. This occurs because their positively charged surfaces interact strongly with the negatively charged cell membrane, leading to cell lysis. To improve safety and compatibility, modifications such as PEGylation and glycosylation are commonly used. These surface alterations reduce toxicity and enhance the overall biocompatibility of dendrimers.

A wide range of dendrimer-based nanocarriers is currently used in cancer therapy, including poly(amidoamine), poly-L-lactide, polylysine, peptide dendrimers, poly (propylene imine), polycaprolactone, and polyethylene glycol-based systems. These dendrimers can encapsulate or attach various anticancer drugs such as paclitaxel, doxorubicin (DOX), methotrexate, and cisplatin. In addition to drug delivery, dendrimers can also incorporate imaging agents like iron oxide nanoparticles and gold nanoparticles, making them useful for diagnostics and tumour visualization.

Attaching specific targeting molecules to dendrimers enhances their ability to recognize and bind to cancer cells. This targeted approach increases treatment effectiveness, reduces toxicity, and helps minimize the adverse effects associated with chemotherapy. Commonly used targeting ligands include galactose, dextran, and folate, along with tumour-specific antigens. (refer fig 3.2)

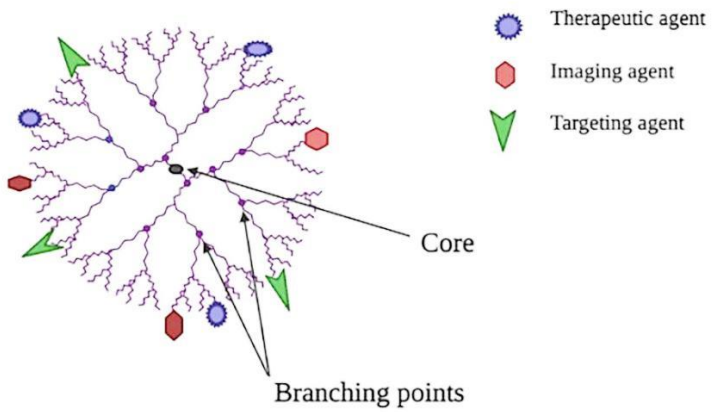


Figure 3.2 - Structure of Dendrimer

3.3 Micelles

Polymeric micelles have gained considerable attention as nanocarriers for cancer diagnosis and treatment. They are formed by the self-assembly of amphiphilic block copolymers into spherical nanostructures, typically 10–100 nm in diameter, consisting of a hydrophobic inner core and a hydrophilic outer shell. The hydrophobic core allows effective encapsulation of water-insoluble anticancer drugs. For targeted delivery, micelle surfaces can be functionalized with ligands such as peptides, aptamers, antibodies, carbohydrates, or folic acid, enabling them to bind selectively to tumour cell receptors. Stimuli-responsive micellar systems are also being widely explored; these systems release their drug cargo in response to triggers like enzymes, temperature changes, ultrasound, oxidation, or pH gradients. In particular, pH-sensitive micelles release their active drugs when exposed to the acidic tumour microenvironment. Multifunctional micelles capable of co-delivering multiple therapeutic agents play an important role in producing synergistic effects in cancer treatment. For example, temperature-responsive micelles reported by Seo and colleagues can simultaneously deliver genetic materials and anticancer drugs. Additionally, polyion complex (PIC) micelles are being

extensively studied for efficient delivery of genes and siRNAs, offering promising avenues for advanced gene-based cancer therapies. (refer fig 3.3)

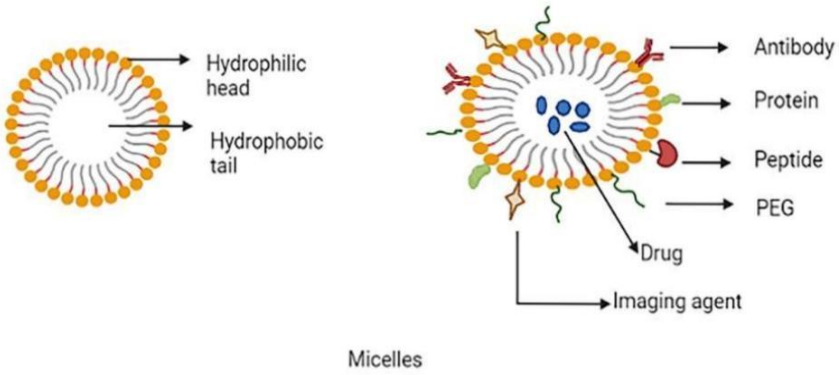


Fig 3.3 - Schematic Representation of Multifunctional Micelles.

3.4 Carbon Nanotubes (CNTs)

Carbon nanotubes (CNTs) are cylindrical, carbon-based nanostructures widely explored as drug carriers in cancer therapy. They are formed from graphene sheets rolled into seamless tubes, giving them an exceptionally high aspect ratio. CNTs can have diameters as small as 1 nm, while their lengths may extend to several micrometres. Depending on their structure, the tubes may be either open-ended or capped.

CNTs exist in two main forms:

- **Single-walled carbon nanotubes (SWCNTs)** – composed of a single graphene cylinder
- **Multi-walled carbon nanotubes (MWCNTs)** – made up of multiple concentric graphene cylinders arranged in a nested fashion

SWCNTs generally possess smaller diameters and greater flexibility, making them suitable for applications such as imaging. MWCNTs, with their larger surface area, allow more efficient internal loading (endohedral filling), which is advantageous for drug delivery. Among various carbon-based nanomaterials, CNTs have gained significant attention due to their unique features, including excellent intracellular uptake, high cargo-loading capacity, and extremely high aspect ratio. These properties make them promising multifunctional nanocarriers for transporting therapeutic agents to cancer cells. (refer fig 3.4)

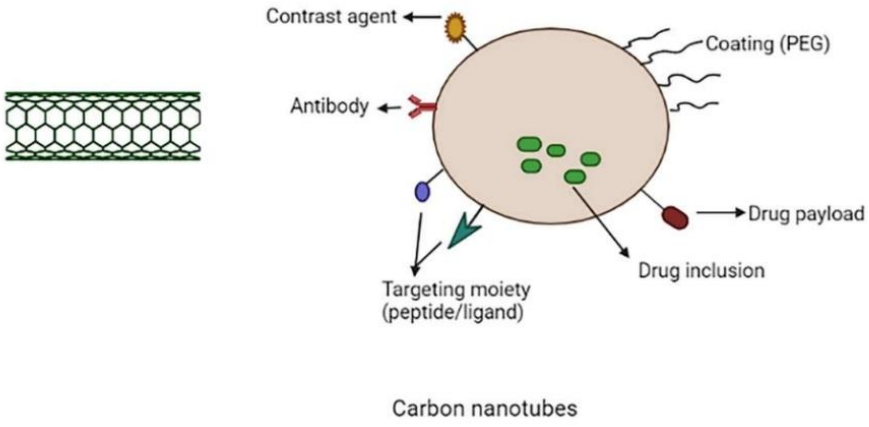


Fig 3.4 - Schematic Representation of Multifunctional Carbon Nanotubes

3.5. Gold Nanoparticles (AuNPs)

Gold nanoparticles (AuNPs) have gained significant scientific attention as versatile nanocarriers in cancer therapy. Their unique structural and optical properties make them valuable for drug delivery, tumour detection, and use as photothermal agents. AuNPs are increasingly preferred in cancer treatment and diagnostic applications because they are chemically inert and exhibit minimal reactivity with biological systems an advantage over many conventional metal-based drug delivery materials. Inorganic nanoparticles, including AuNPs, possess stable physicochemical characteristics that allow them to convert light or radiation energy into reactive species. This ability is particularly useful in photodynamic and photothermal therapies designed to destroy solid tumours. Beyond therapeutic applications, these nanoparticles play key roles in drug formulation, bioimaging, and biosensing due to their stability and tunable surface properties. When engineered to the appropriate size and shape, AuNPs are generally non-toxic and exhibit low phototoxicity, further supporting their suitability as nanocarriers in targeted cancer treatment.

Gold nanoparticles (AuNPs) have gained significant research interest due to their unique optical properties, tunability, and strong surface plasmon resonance. These nanoparticles can be readily modified by altering their surface characteristics, including the introduction of negative charges. This tunability allows AuNPs to be easily functionalized with a wide range of molecules such as ligands, drugs, and genes.

In addition to their adaptability, AuNPs exhibit excellent biocompatibility and minimal toxicity, making them highly suitable as drug-delivery carriers. For example, methotrexate (MTX) conjugated with gold nanoparticles has demonstrated greater cytotoxicity against various tumour cell lines compared to free MTX. When delivered through AuNPs, MTX accumulates more rapidly and at higher concentrations within tumour cells. Similarly, doxorubicin linked to AuNPs through an acid-labile bond has shown enhanced toxicity in multidrug-resistant MCF-7/ADR breast cancer cells, indicating improved therapeutic efficiency.

PEGylation of gold nanoparticles offers an additional advantage by reducing uptake by the reticuloendothelial system (RES), thereby enhancing circulation time. PEGylated AuNPs show improved stability and solubility under physiological conditions. Their surfaces can be further engineered with targeting ligands for precision drug delivery. For instance, fluorescent heparin-conjugated AuNPs can support cancer diagnostics, while transferrin-linked AuNPs enable targeted drug delivery.

Gold nanoparticles also enhance photodynamic therapy outcomes. Xin et al. developed a delivery system for phthalocyanine chloride tetrasulfonic acid (AlPcS4) using AuNPs. Because AuNPs provide high accessibility for AlPcS4 and promote accelerated singlet oxygen generation, they induce strong photothermal effects and potent anti-tumour activity. (refer fig 3.5)

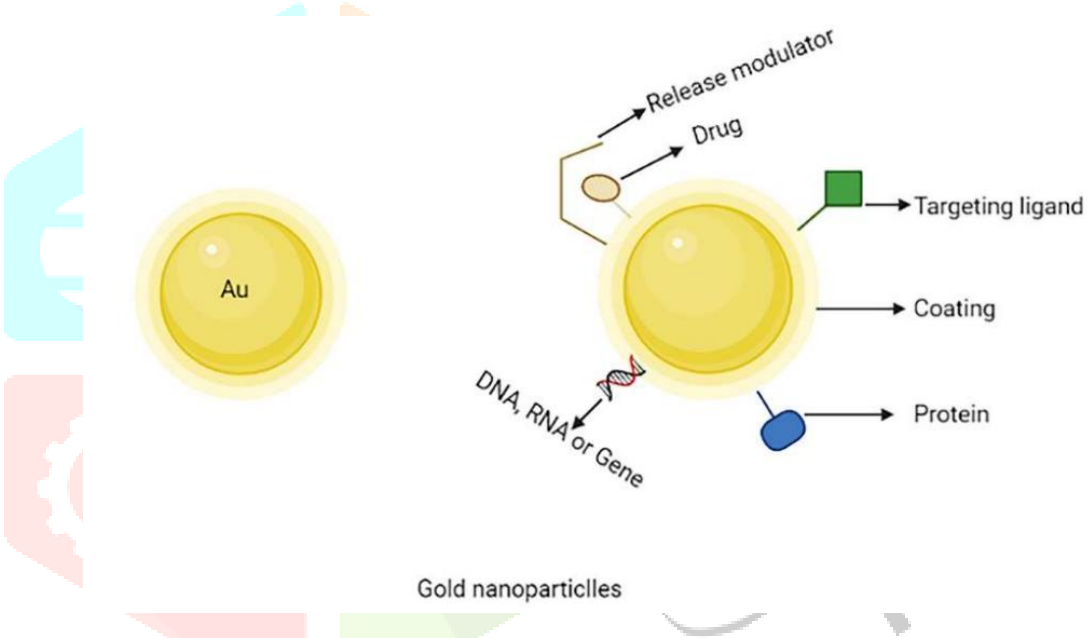


Fig 3.5 - Schematic Representation of Multifunctional Gold Nanoparticles.

4. Types of Targeting Moieties

Targeting moieties play a crucial role in enhancing the specificity of nanocarrier-based drug delivery systems in cancer therapy. These targeting molecules are commonly attached to the surface of nanocarriers through physical adsorption or chemical conjugation. A variety of biological and synthetic entities including peptides, proteins, nucleic acids, carbohydrates, vitamins, and other small molecules are used for this purpose.

4.1 Aptamer-Based Targeting

Aptamers are short, single-stranded nucleic acid ligands (DNA or RNA) capable of binding selectively and with high affinity to specific molecular targets. They are typically identified using the SELEX (Systematic Evolution of Ligands by Exponential Enrichment) technique. One prominent example of aptamer-based targeting is the delivery of cisplatin to prostate cancer cells using aptamer-functionalized nanocarriers. Among the aptamers widely studied in cancer research, AS1411, a single-stranded DNA aptamer, is particularly notable. AS1411 has been shown to inhibit the growth of various human cancer

cell lines, including prostate, breast, and lung cancers. To enhance intracellular delivery and therapeutic efficiency, nanocarriers such as aptamer-conjugated gold nanospheres (Apt-AuNS) have been used to improve the stability and bioactivity of AS1411.

4.2 Small Molecule-Based Targeting

Small molecules are advantageous as targeting moieties because they are easy to synthesize, cost-effective, and structurally diverse. Among these, folate (vitamin B9) is one of the most frequently investigated targeting molecules. Folate receptors are overexpressed in many tumour cells due to their increased need for rapid growth and division, especially during development. Another important small molecule is riboflavin (vitamin B2), which plays a vital role in cellular metabolism. Tumour cells often exhibit elevated levels of riboflavin carrier protein (RCP). As a result, flavin mononucleotide (FMN) a natural ligand of RCP has been used to actively target tumour and endothelial cells. A notable example of small molecule-mediated delivery is the development of lactose–doxorubicin (Lac-DOX) nanocarriers. These nanoparticles demonstrate improved anticancer activity with reduced side effects through a combination of passive and active targeting. Importantly, Lac-DOX nanoparticles exhibit very low systemic toxicity, as shown by minimal uptake in healthy tissues and normal biochemical profiles in vivo.

4.3 Peptide-Based Targeting

Peptides are highly suitable targeting ligands due to their small size, low cost, ease of synthesis, and minimal immunogenicity. They are often derived from the active binding domains of specific proteins or receptors. A commonly cited example is ANGIOPEP-2, a peptide that targets the low-density lipoprotein receptor related protein (LRP). This receptor is overexpressed in glioblastoma multiforme and is also present on the blood–brain barrier (BBB). When conjugated to nanocarriers, ANGIOPEP-2 enables efficient transport across the BBB, facilitating targeted delivery of therapeutics to brain tumours such as gliomas conditions that are otherwise difficult to treat due to restricted drug penetration.

4.4 Antibody-Based Targeting

Antibodies have emerged as powerful targeting moieties because they possess two antigen-binding sites, allowing them to bind with exceptional affinity and specificity to tumour-associated antigens. Several clinically approved monoclonal antibodies have been successfully used in cancer therapy. For example:

- Rituximab, approved by the FDA for the treatment of non-Hodgkin’s lymphoma, targets the CD20 antigen on B-cells.
- Bevacizumab, an anti-VEGF monoclonal antibody, is used to treat metastatic colorectal, breast, and lung cancers. It suppresses tumour angiogenesis by binding to and neutralizing soluble vascular endothelial growth factor (VEGF), thereby preventing VEGF from interacting with its receptor VEGFR-2.

These antibodies can also be conjugated to nanoparticle surfaces to achieve selective targeting of tumour cells, reducing off-target toxicity and enhancing therapeutic effectiveness.

5. Stimulus for Drug Release

Stimuli-responsive drug delivery systems are engineered to release therapeutic agents only when triggered by specific signals. These stimuli are broadly classified into endogenous stimuli (generated within the body) and exogenous stimuli (applied externally). Exogenous stimuli include temperature changes, electric fields, magnetic fields, and ultrasonic waves each serving as an external trigger for drug release from smart nanocarriers.

Endogenous stimuli, on the other hand, arise naturally inside the body and include variations in pH, enzyme activity, temperature, and redox conditions. These biological differences between healthy and tumour tissues make endogenous stimuli particularly valuable in cancer therapy.

5.1 Endogenous Stimulus

Endogenous (intrinsic) stimuli originate from physiological conditions within the body. Internal factors such as enzyme activity, pH gradients, and redox potential can be exploited to activate drug release at tumour sites. This approach ensures high targeting precision and minimizes drug exposure to healthy tissues.

a) pH-Responsive Stimulus Drug Delivery Systems (DDS)

According to the Warburg effect, tumour cells rely heavily on glycolysis for energy production, even in the presence of oxygen. This leads to excess lactic acid generation and results in an acidic tumour microenvironment.

Key pH characteristics include:

- **Normal tissues:** ~pH 7.4
- **Tumour extracellular environment:** ~pH 6.5 (acidic)
- **Intracellular organelles:**
  - Lysosomes: pH 4–5
  - Endosomes: pH 5–6
  - Golgi complex: pH ≈ 6.4

These pH variations between healthy cells and tumour cells provide a strong foundation for the development of pH-responsive nanocarriers.

Two major strategies are used in pH-responsive DDS:

1. Polymers that undergo structural changes (e.g., conformational shifts or dissolution) in response to acidic pH.
2. Nanocarriers containing acid-labile linkages, which break down in acidic environments, resulting in rapid drug release specifically at tumour sites.

b) Redox-Sensitive Stimulus DDS

Redox-responsive systems take advantage of the distinct redox conditions in tumour cells. Tumour tissues contain significantly higher levels of reducing agents such as:

- Glutathione (GSH)
- Vitamin E
- Vitamin C

These molecules help maintain intracellular redox balance but also serve as natural triggers for redox-sensitive nanocarriers. Such nanocarriers are used for the controlled release of anticancer drugs, genes, proteins, and even for ultrasound imaging.

5.2 Exogenous Stimulus

Exogenous stimuli are externally applied physical signals such as ultrasound, temperature changes, magnetic fields, or light. When these signals interact with specially designed nanocarriers, they can induce rapid and localized drug release.

a) Temperature-Responsive Stimulus DDS

Temperature-sensitive nanocarriers such as liposomes, nanoparticles, and polymeric micelles respond to changes in temperature. When the temperature rises above the polymer's critical solution temperature (CST), the hydrophilic–hydrophobic balance shifts, leading to:

- polymer chain dehydration
- structural alteration of the carrier
- subsequent drug release

An example is the thermo-responsive system developed by Allam et al., where camptothecin-loaded superparamagnetic nanoparticles (SPIONs) were coated with DPPC and DPPG. Under magnetic hyperthermia:

- solubility and stability improved,
- and the system demonstrated significantly higher cytotoxicity toward cancer cells compared to free camptothecin.

b) Light-Responsive Delivery Systems

Light-responsive DDS release their drug payload when exposed to external light sources such as UV, visible, or near-infrared (NIR) radiation. For instance, doxorubicin-loaded gold nanocarriers show enhanced drug release under 808 nm NIR illumination. In another study, Zhang et al. developed PEGylated liposomes coated with doxorubicin-loaded mesoporous carbon nanocomposites for chemo-photothermal therapy in breast cancer. Under NIR irradiation:

- drug release was significantly accelerated,
- the system selectively targeted breast cancer cells, and
- toxicity studies showed minimal adverse effects on normal cells.

6. Nanomedicines: Development, Cost-Effectiveness and Commercialization

Although nanotechnology and nanocarrier-based drug delivery systems have gained significant scientific attention and show strong potential for medical applications, there remains a considerable gap between technological advancement and successful market commercialization. At present, most commercialized nanotherapeutic products are driven by start-ups or small/medium enterprises, rather than major pharmaceutical companies. Large pharma companies show limited investment interest in emerging nanomedicine technologies, making it challenging for smaller developers to find suitable industry partners willing to license and launch these nanotherapeutics. Another major challenge is the high per-unit cost of nanomedicines. Nanotherapeutic manufacturing often faces diseconomies of scale, meaning that large-scale production is difficult and expensive. This results in high acquisition costs for nanomedicines, creating barriers to their widespread clinical adoption. Additionally, because the financial returns are relatively low, companies struggle to recover their research and development investments. These factors together represent a major obstacle to sustainable commercialization and long-term market success of nanotherapeutics. Despite these concerns, nanomedicines can still provide significant economic benefits. Their ability to reduce side effects and improve therapeutic efficiency can save costs related to additional medical procedures, extended hospital stays, and healthcare personnel.

Moreover, patients experience faster recovery and can return to work sooner, offering broader socio-economic advantages. These indirect savings can help balance the initially high acquisition costs of nanotherapeutic products. To enhance the acceptance and commercialization of nanomedicines, standardized cost-effectiveness analyses are crucial. Such studies can demonstrate the overall value of nanotherapeutics and make them more appealing for investment by large pharmaceutical firms. Recent cost-effectiveness assessments, for example, have shown that nanomedicines used in ovarian cancer therapy are not only highly cost-effective but also cost-saving for the healthcare system and society. Therefore, expanding such economic evaluations across various types of nanotherapeutics will be essential. This will help secure better reimbursement policies, encourage higher investments, and ultimately support smooth and successful commercialization of nanomedicine products.

7. Future Perspectives in Cancer Treatment

Nanomedicine has progressed rapidly in recent years, and its contribution to cancer therapy continues to expand. Engineered nanoparticles capable of targeted drug delivery, especially when integrated with controllable triggering mechanisms, are expected to significantly transform future cancer treatments. However, cancer remains a highly complex, heterogeneous, and multifactorial disease. Many cancer types still have unclear origins, and the biological behaviour of tumours often varies widely among patients. This diversity demands personalized and adaptable therapeutic strategies, which remains a major challenge in oncology.

Stimuli-responsive nanostructures and DNA-based nanocarriers represent promising tools for addressing this challenge. Stimulus-sensitive DNA nanostructures, particularly hybrid systems, offer exceptional specificity, programmability, and multifunctionality for targeted drug delivery and tumour diagnostics. These systems have been widely investigated and show great potential to enhance cancer treatment efficiency while minimizing undesired toxicity to healthy tissues. In addition, cancer immunotherapy has emerged as a powerful therapeutic avenue capable of modulating the immune response against tumours. The development of cancer vaccines using customizable polymeric nanoparticles is especially promising. Such nanoparticles can be engineered to stimulate multiple anti-tumour immune pathways, providing an innovative alternative to current immunotherapy approaches.

Overall, the combination of polymeric nanoparticles, stimuli-responsive systems, and DNA nanostructures may redefine next-generation cancer therapy. These advanced nanoplatforms hold strong potential for enabling highly personalized, precise, and effective cancer treatment with reduced adverse effects and improved patient outcomes.

Conclusion

Nanotechnology has transformed the landscape of cancer therapy by introducing highly versatile, targeted, and efficient drug delivery systems. The use of functionalized nanocarriers, stimulus-responsive platforms, and ligand-based targeting strategies has significantly improved the precision and therapeutic outcomes of anticancer treatments while reducing systemic side effects. Although nanomedicines exhibit remarkable scientific promise, their translation from laboratory research to large-scale clinical application remains limited due to challenges such as high production costs, complex regulatory pathways, and limited commercialization by major pharmaceutical companies. Strengthening cost-effectiveness studies, optimizing large-scale manufacturing, and establishing clearer regulatory guidelines will be crucial for accelerating their clinical acceptance. The advancements in hybrid nanostructures, DNA-based nanodevices, and nanoparticle-assisted immunotherapy hold tremendous potential in shaping personalized cancer treatment. Tailored polymeric nanoparticles and next-generation cancer vaccines may further broaden the scope of nanomedicine by enabling patient-specific therapeutic approaches. Overall, continued interdisciplinary research, strategic industrial

partnerships, and supportive health policies will be essential to fully realize nanotechnology's transformative impact on cancer care.

References

1. Kenchegowda M, Rahamathulla M, UmmeHani, Begum MY, Guruswamy S, Osmani RAM, Gowrav MP, Alshehri S, Ghoneim MM, Alshlowi A, Gowda DV.
2. Sun L, Cai L, Liu H, Ye Y, Lei Y, Islam R, Tan S, Tong R, Miao Y-B. Smart nanoparticles for cancer therapy. Signal Transduct Target Ther.
3. Yao Y, Zhou Y, Liu L. Nanoparticle-based drug delivery in cancer therapy and its role in overcoming drug resistance. Front Mol Biosci. 2020; 7:193. doi:10.3389/fmolb.2020.00193.
4. Rashidi N, Davidson M, Apostolopoulos V, Nurgali K. Nanoparticles in cancer diagnosis and treatment: Progress, challenges, and opportunities. J Drug Deliv Sci Technol. 2024;105599.
5. Peer D, Hong S. Nanocarriers as an emerging platform for cancer therapy. Nat Nanotechnol. 2007;2(12):751–760. doi:10.1038/nnano.2007.387.
6. Kanamala M, Wilson WR, Yang M, Palmer BD, Wu Z. Mechanisms and biomaterials in pH-responsive tumour-targeted drug delivery: A review. Biomaterials. 2016; 85:152–167.
7. Lee JM, Park H, Oh KT, Lee ES. pH-responsive hyaluronated liposomes for docetaxel delivery. Int J Pharm. 2018; 547:377–384.
8. Anselmo AC, Mitragotri S. Nanoparticles in the clinic: an update. Bioeng Transl Med. 2019;4: e10143.
9. Chang TC, et al. Phase I study of nanoliposomal irinotecan (PEP02) in advanced solid tumor patients. Cancer Chemother Pharmacol. 2015; 75:579–586.
10. Apte RS, Chen DS, Ferrara N. VEGF in signaling and disease: beyond discovery and development. Cell. 2019; 176:1248–1264. doi: 10.1016/j.cell.2019.01.021.
11. Halin C, et al. Enhancement of the antitumor activity of interleukin-12 by targeted delivery to neovasculature. Nat Biotechnol. 2002; 20:264–269.
12. Silverman J, et al. Multivalent avimer proteins evolved by exon shuffling of a family of human receptor domains. Nat Biotechnol. 2005; 23:1556–1561.
13. Sapra P, Allen TM. Ligand-targeted liposomal anticancer drugs. Prog Lipid Res. 2003; 42:439–462.
14. Moghimi SM. Recent developments in polymeric nanoparticle engineering and their applications in experimental and clinical oncology. Anticancer Agents Med Chem. 2006; 6:553–561.