RESEARCH PAPER

Targeted Drug Delivery

Kamali Manickavasagam Lekshmi[1*], Reshath R[1], Sanjith P[1], D Dhivvya Bhalan[1], Asma J[1]

[1] Department of Biotechnology, KIT-Kalaignarkarunanidhi Institute of Technology, Coimbatore, Tamil Nadu, India.

[*] Kamali Manickavasagam Lekshmi. ORCID ID: 0000-0002-2912-8337. Email: kamalikitbt@gmail.com
Reshath R. ORCID ID: 0009-0004-6865-8201. Email: reshathrs2004@gmail.com
Sanjith P. ORCID ID: 0009-0007-7100-9394. Email: sanjithvk2004@gmail.com
D Dhivvya Bhalan. ORCID ID: 0009-0001-3948-1716. Email: j.duraivelan@gmail.com
Asma J. ORCID ID: 0009-0008-9733-714X. Email: asmajam2004@gmail.com

---

ABSTRACT

The emergence of nanotechnology has revolutionized modern drug delivery by enabling precise, targeted, and sustained therapeutic release through engineered nanocarriers. Unlike conventional dosage forms, nanocarriers such as liposomes, polymeric nanoparticles, micelles, dendrimers, nanogels, and hybrid systems offer tunable physicochemical properties that enhance bioavailability, reduce systemic toxicity, and optimize pharmacokinetics. These nano systems exploit mechanisms such as passive and active targeting, stimuli-responsive release, and controlled degradation to overcome biological barriers and improve drug localization at diseased sites. Moreover, the fusion of nanocarriers with advanced biopolymers, ligands, and stimuli-sensitive components has expanded their clinical potential in cancer therapy, infectious diseases, and regenerative medicine. The convergence of material science, molecular biology, and nanotechnology thus continues to shape next-generation therapeutics by translating nanoscale precision into real-world biomedical applications. This review underscores the innovative strategies, mechanisms, and future directions that define nanocarrier-mediated drug delivery as a cornerstone of personalized and precision medicine.

Keywords: Nanocarriers, Targeted Drug Delivery, Nanotechnology, Controlled Release, Precision Medicine

How to cite this article: Kamali Manickavasagam Lekshmi, Reshath R, Sanjith P, D Dhivvya Bhalan, Asma J. Targeted Drug Delivery. Int J Drug Deliv Technol. 2026;16(37s): 313-330. DOI: 10.25258/ijddt.16.37s.41

Source of support: Nil.

Conflict of interest: None

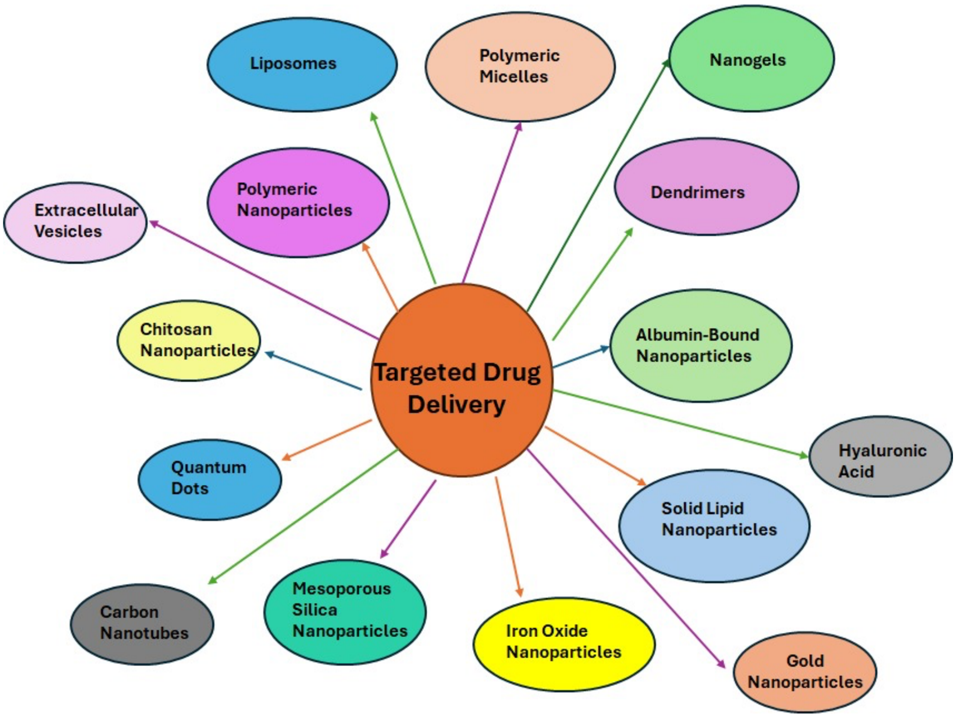

Figure 1: Graphical abstract

Introduction

Targeted drug delivery defines a pivotal change in modern pharmacology, linking nanotechnology, biomaterials, and molecular biology to create site-specific and controlled therapeutic systems. Unlike conventional formulations that distribute drugs indiscriminately, targeted delivery confines the drug to the affected cells while sparing bystander cells, thereby improving efficacy, reducing systemic toxicity, and enhancing patient safety(Guimarães et al., 2021). This concept converts drug administration from a passive process into an engineered and intelligent mechanism that responds to biological signals and releases its therapeutic content at the right place in a controlled manner.

Nanocarrier-based systems such as liposomes, polymeric nanoparticles, micelles, dendrimers, nanogels, and hybrid carriers, stand at the center of this transformation(Guimarães et al., 2021)(Begines et al., 2020). Their ability to encapsulate and protect active molecules while controlling their pharmacokinetic behaviour redefines the pharmacodynamic parameters as well. Each carrier type possesses distinctive physicochemical characteristics size, charge, surface chemistry, and degradability that determine circulation half-life and cellular uptake(Sharma et al., 1997)(Castro et al., 2022). Through precise control of these properties, nanocarriers overcome barriers such as enzymatic degradation, renal clearance, poor membrane permeability and low drug retention.

Liposomes were the first nanocarriers to demonstrate reliable performance in clinical medicine. Built from phospholipids and cholesterol, they resemble natural cell membranes and accommodate both hydrophilic and hydrophobic drugs(Guimarães et al., 2021). Their amphiphilic bilayer protects unstable molecules and increases bioavailability. The introduction of PEGylated *stealth liposomes* extended blood circulation and reduced clearance by the immune system(Yadav et al., 2017). Further innovations led to *targeted liposomes*, which use surface-bound ligands to recognize and bind to diseased cells, and *stimuli-responsive liposomes* that release drugs when triggered by pH, temperature, or enzymatic activity(Sharma et al., 1997). Advanced microfluidic and supercritical fluid techniques now ensure consistent liposome size, stability, and drug-loading capacity, turning them into dependable carriers for cancer and infection therapies.

Polymeric nanoparticles represent the next stage of precision delivery. Constructed from biodegradable polymers such as polylactic acid (PLA), polyglycolic acid (PGA), and PLGA, these nanosystems maintain drug stability, prolong release, and achieve specific localization within tissues(Begines et al., 2020)(Castro et al., 2022). Their synthesis by emulsification, solvent evaporation, or ionic gelation allows control of particle size and homogeneity (Liu et al., 2025). *Stimuli-responsive polymeric nanoparticles*, often called smart nanocarriers, detect environmental cues acidic pH, heat, or magnetic fields, and discharge drugs only in targeted microenvironments(Begines et al., 2020). This engineered responsiveness produces exact pharmacological control while eliminating unwanted side effects.

Polymeric micelles expand this concept further. Formed by self-assembly of amphiphilic block copolymers, they feature a hydrophobic core that solubilizes poorly water-soluble drugs and a hydrophilic shell that ensures stability in physiological fluids(Negut et al., 2023). The Enhanced Permeability and Retention (EPR) effect allows micelles to accumulate passively within tumor tissues (Atanase, 2021). Surface modification with ligands or antibodies provides active targeting, ensuring selective uptake by cancer cells (Gong et al., 2012). Controlled release, triggered by local pH or external stimuli, enhances therapeutic precision and minimizes toxicity (Q. Wang et al., 2023). Polymeric micelles combine biocompatibility, long circulation, and high specificity, positioning them as vital tools in oncological nanomedicine (Negut et al., 2023)(Atanase, 2021).

Dendrimers provide a structurally perfect alternative for multifunctional drug delivery. Their tree-like, monodisperse architecture contains a central core, interior branches, and multiple terminal groups that serve as binding sites for drugs, peptides, or imaging agents (J. Wang et al., 2022). This uniform structure guarantees predictable pharmacological behavior and high loading efficiency. Dendrimer conjugation improves the solubility and permeability of poorly soluble drugs, achieving controlled release through chemical or electrostatic bonding (Fadaei et al., 2025)(Naji et al., 2022). In cancer and neurological therapy, dendrimers cross biological barriers such as the blood–brain barrier and deliver their cargo directly to target cells, maintaining therapeutic levels while minimizing toxicity (J. Wang et al., 2022)(Naji et al., 2022).

Nanogels integrate hydrogel softness with nanoscale precision. Their three-dimensional polymeric network retains high water content and provides exceptional biocompatibility and swelling-controlled release (Suhail et al., 2019). In transdermal systems, nanogels enhance drug penetration and provide steady release without the gastrointestinal side effects of oral therapy (Vashist et al., 2024)(S et al., 2024). Vaginal nanogels deliver antimicrobial and antiretroviral drugs with localized retention and minimal irritation (Suhail et al., 2019)(S et al., 2024). Their flexibility, responsiveness, and safety confirm their position as next-generation topical delivery vehicles (Delgado-Pujol et al., 2025).

Hyaluronic acid (HA)–based carriers add biological selectivity to drug delivery. HA binds specifically to CD44 receptors, overexpressed on many tumor cells, ensuring that the drug accumulates directly in cancerous tissue (Pashkina et al., 2025). HA-drug conjugates such as Oncofid-P for bladder carcinoma have entered clinical practice, proving their effectiveness and safety (Fu et al., 2023). HA maintains its biodegradability while enabling multifunctional designs that combine drug delivery with imaging or gene therapy (Pashkina et al., 2025)(Salari et al., 2021). By coupling HA with targeting ligands or siRNA, researchers achieve simultaneous chemotherapeutic and gene-silencing effects, intensifying tumor suppression without harming normal cells (Pashkina et al., 2025).

Albumin nanoparticles provide a natural, clinically validated platform for targeted and controlled delivery. Human serum albumin (HSA) binds a broad range of therapeutic molecules and circulates for extended periods without immunogenicity (Meng et al., 2022). Drugs such as paclitaxel in Abraxane utilize albumin nanoparticles to improve solubility and tumor uptake through receptor-mediated endocytosis(Qu et al., 2024). These carriers integrate stability, safety, and versatility, allowing efficient delivery in oncology and inflammatory diseases.

Solid lipid nanoparticles (SLNs) merge lipid compatibility with structural stability, serving as excellent vehicles for both hydrophilic and lipophilic drugs (Mirchandani et al., 2021). Their solid matrix ensures sustained release and superior protection of encapsulated drugs. SLNs improve absorption across biological barriers, enhance oral and brain bioavailability, and reduce toxicity in prostate and brain cancer treatments (Akanda et al., 2023)(Satapathy et al., 2021)(Mendoza-Muñoz et al., 2021). Their high stability and non-toxic lipid content make them suitable for chronic and controlled therapy.

Inorganic nanocarriers such as gold, iron oxide, and mesoporous silica nanoparticles extend targeted drug delivery into diagnostic and theranostic domains. Gold nanoparticles (GNPs) bind chemotherapeutics, nucleic acids, and antibodies, enabling site-specific release and optical tracking through their distinctive plasmonic properties (Khlebtsov et al., 2011)(Ramadan et al., 2025)(Lopes-Nunes et al., 2021). Iron oxide nanoparticles (IONs) allow magnetic field–guided targeting and hyperthermia treatment, concentrating drugs precisely at the tumor site while simultaneously enabling magnetic resonance imaging (Stanicki et al., 2022)(Estelrich et al., 2015)(Qiao et al., 2023). Mesoporous silica nanoparticles (MSNs), with adjustable pore size and large surface area, co-deliver drugs and genes while providing pH-controlled release, leading to superior anticancer activity with minimal side effects (Santhamoorthy et al., 2025)(Khalbas et al., 2024).

Carbon nanotubes, quantum dots, and chitosan nanoparticles represent the diversity of nanoscale design. Carbon nanotubes exhibit remarkable drug-loading capacity and efficiently transport chemotherapeutics across cell membranes, particularly in breast and lymphatic cancer treatment (Zhang et al., 2011)(Achar et al., 2025). Quantum dots combine delivery and imaging functions, enabling real-time tracking of therapeutic progress (Hamidu et al., 2023). Chitosan nanoparticles, due to their mucoadhesive and biodegradable nature, enhance drug absorption in ocular and oral applications, ensuring sustained and localized effect (Obeidat et al., 2025)(Stefanache et al., 2025).

The most recent advancement, extracellular vehicles (EVs), utilizes nature-derived nanosystems for precision therapy. EVs carry proteins, lipids, and nucleic acids across biological barriers with inherent biocompatibility (Verma et al., 2025). Their surfaces can be engineered with targeting ligands or magnetic nanoparticles to achieve highly selective tumor localization (Rawat et al., 2025)(Langellotto et al., 2024)(Herrmann et al., 2021). Integration with biomaterials such as hydrogels further extends their stability and controlled-release capacity, allowing continuous therapeutic action at the disease site (Rawat et al., 2025).

Targeted drug delivery stands as the cornerstone of precision and personalized medicine. It transforms pharmacotherapy into a programmable science of accuracy, predictability, and control. Nanocarriers provide unmatched capability to transport, protect, and release drugs exactly where needed, aligning pharmacological effect with biological demand (Guimarães et al., 2021)(Begines et al., 2020)(Pashkina et al., 2025)(Qu et al., 2024)(Santhamoorthy et al., 2025). With the convergence of nanotechnology, molecular design, and clinical translation, targeted drug delivery no longer represents a futuristic concept but a mature technology that defines the modern era of intelligent therapeutics.

Liposomes:

Liposomal formulation is achieved by choosing a targeting strategy, functionalization, and adequate liposome composition, as they developed deeper in the section(Guimarães et al., 2021). The following selection of phospholipids, head group, and chain length, and also the ratio of the liposomes' components, are crucial features to determine the safety, stability, and efficiency of liposomes. The number and the rigidity of liposomes as the drug delivery system are affected by size, surface charge, lipid organization, and surface modification. The main components of liposomes are glycerophospholipids, which are amphiphilic lipids composed of a glycerol molecule bound. In this organic group, natural phospholipids are classified **as** phosphatidic acid (PA), phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylinositol (PI), phosphatidylglycerol (PG), and phosphatidylserine (PS). This group has a strong ability to form a stable bilayer due to their amphipathic character (Guimarães et al., 2021)(Yadav et al., 2017). This structure allows them to carry both hydrophilic drugs in the core and the hydrophobic drugs within the lipid layer, which will protect medicines from degradation and improve their circulation time in character(Sharma et al., 1997).

Liposomes depend on the phospholipids, cholesterol content, size, surface charge, and temperature, which together influence stability and efficiency. Liposomes can be classified as unilamellar(ULV), multilamellar (MLV) multivesicular vesicles (MLV), depending on their number of bilayers and size(Guimarães et al., 2021). Their size range is divided into 3 categories: small unilamellar vesicles (SUVs, 20 – 100 nm), large unilamellar vesicles (LUVs, >100 nm), and giant unilamellar vesicles (GUVs, >1000 nm) [FIG 1]. It also explains the method of liposome preparation and advanced methods like supercritical fluid and microfluidics techniques. These methods affect the size, drug loading, and the stability of the final liposomes (Sharma et al., 1997)(Guimarães et al., 2021).

Before using, liposomes are tested for their size, shape, drug content, and the release rate to check if they are working properly. Based on surface modifications, liposomes can be conventional, stealth (PEGylated), targeted, or stimuli responsive. Stealth liposomes stay longer in the bloodstream, targeted liposomes deliver drugs directly to diseased cells, and stimuli-responsive liposomes release drugs when triggered by pH or temperature changes(Yadav et al., 2017).

In the past years, liposomes have improved design by adding polymers, antibodies, and ligands on their surface to increase accuracy and control. These functionalized liposomes can recognize specific cells, such as cancer cells, and deliver the drug specifically where it is needed (Sharma et al., 1997)(Yadav et al., 2017). The targeted delivery reduces side effects and increases the effectiveness of the treatment. Nowadays, liposomes are also being mixed with diagnostic and imaging substances to create theranostic liposomes, which have applications in both disease diagnosis and treatment(Guimarães et al., 2021).

They also had major problems like instability, oxidation, and difficulty in large-scale production. Freeze-drying with sugar stabilizers has helped to improve their shelf life(Sharma et al., 1997) .

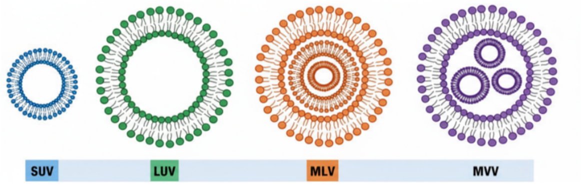

Figure 2: Liposomal classification based on lamellarity and size. SUV (Small Unilamellar Vesicles), LUV (Large Unilamellar Vesicles), MLV (Multilamellar Vesicles) and MVV (Multi Vesicular Vesicles) (Guimarães et al., 2021).

Polymeric Nanoparticles:

Polymeric nanoparticles have emerged as one of the most promising tools in modern drug delivery, providing modern possibilities for precision medicine. These nano-sized carriers range from 10 to 500 nanometers(Begines et al., 2020). This design allows for improved drug stability, reduced side effects, and enhanced bioavailability. It is the nanoparticles for biomedical applications, including anti-microbial activity and controlled drug release (Castro et al., 2022). The term nanoparticle includes nanocapsules and nanospheres, which differ according to their composition and structural organization, as illustrated in Drug transport systems containing polymeric nanoparticles have at least 100 nm in diameter, with most of them falling between 100 and 500 nm. Biodegradable synthetic polymers are systems applied for the controlled and targeted delivery of drugs, especially polylactic acid (PLA), polyglycolic acid (PGA), and lacticoglycolic acid (PLGA) derived polymers that exhibit characteristics of biodegradability and biocompatibility(Begines et al., 2020)(Castro et al., 2022).

From the conventional method of the performed polymers (emulsification-solvent evaporation, salting-out, dialysis, ionic gelation, solvent emulsification-diffusion). Emulsification-solvent evaporation is detailed, noting parameters like solvent type, polymer concentration, and surfactant influence on particle size and homogeneity (Liu et al., 2025). Meanwhile, in the Drug Encapsulation, the transport device should have biocompatibility, particle reduced size, high drug-loading-rate, and/or drug encapsulation and entrapment efficiency. The two ways have occurred in the encapsulation, either by incorporating the drug at the time of nanoparticle formulation or by adsorption/absorption of the drug after the nanoparticle formation. during synthesis via adsorption/absorption, ideally near the isoelectric point for high efficiency (73–87% for betamethasone in chitosan-hyaluronic acid nanoparticles.Including curcumin in the PLGA increases 80% efficiency, pointing to polymer-drug interactions and functional groups as critical for solubility and stability (Castro et al., 2022)(Liu et al., 2025).

Stimuli-responsive polymeric nanopoparticle, referred to as “smart nanocarriers”. These systems can sense environmental changes such as pH, temperature, magnetic fields, light, ultrasound, or enzyme activity, triggering the release of drugs only under specific physiological or pathological conditions (Begines et al., 2020). Such responsiveness enables precise delivery to diseased tissues, particularly tumors or inflamed regions, thereby enhancing therapeutic efficiency while minimizing toxicity. Controlled drug release mechanisms, which depend on the polymer degradation, diffusion rates, and matrix composition. From both passive and active targeting, these nanoparticles achieve prolonged circulation and selective accumulation at the target site. Meanwhile addition of chitosan-based nanoparticles demonstrates mucoadhesive and antimicrobial properties, which improve the absorption across biological barriers and the extended retention(Begines et al., 2020)(Liu et al., 2025).

polymeric nanoparticles represent a transformative advancement in pharmaceutical technology. Their versatility, tunable properties, and responsiveness to biological stimuli make them a cornerstone in the development of next-generation therapeutics (Castro et al., 2022).

Polymeric Micelles:

Polymeric micelles have gained significant attention as nanoscale carriers for targeted drug delivery. These structures are formed from amphiphilic block copolymers that spontaneously arrange into a core–shell configuration in aqueous environments (Negut et al., 2023)(Q. Wang et al., 2023). The majority of polymeric micelles have hydrophobic small molecules designed with the intention of delivering hydrophobic anticancer drugs. Micelles can protect medications from oxidation in both in vitro and in vivo environments due to their core-shell structure (Negut et al., 2023). Polymeric micelles depend on the chemical composition, molecular weight, and ratio of the hydrophobic and hydrophilic segments. Common polymers used include polyethylene glycol (PEG), poly (lactic acid) (PLA), polycaprolactone (PCL), and poly (lactic-co-glycolic acid) (PLGA). These materials are valued for their biocompatibility, biodegradability, and minimal toxicity (Gong et al., 2012)[Fig 2].

It is particularly suited for Drug delivery because of its ability to build up in diseased tissues through the Enhanced Permeability and Retention (EPR) effect (Atanase, 2021). This allows them to passively target tumor tissues by taking advantage of the vasculature of cancer cells, and by improving drug accumulation at the site while reducing systemic toxicity. Moreover, the hydrophilic corona, often made of polyethylene glycol (PEG), prevents recognition by the immune system and extends circulation time, enhancing overall therapeutic performance (Atanase, 2021)(Kotta et al., 2022). The stimuli-responsive drug can be released slowly over time by pH, temperature present in the internal stimuli, light, ultrasound, and magnetic fields in the external stimuli (Kotta et al., 2022). This controlled release mechanism offered a greater efficiency and reduced systemic toxicity (Q. Wang et al., 2023).

In active targeting, the functionalized polymeric micelles are attached to the ligands, antibodies, or peptides to the micelle surface (Gong et al., 2012). It is designed that carriers specifically recognize receptors overexpressed on cancer or diseased cells. This significantly enhanced active targeting to improve cellular uptake and therapeutic response. Polymeric micelles face challenges in clinical translation, including limited drug-loading capacity and instability during storage (Gong et al., 2012). These Drug deliveries represent a versatile, biocompatible platform for the delivery of drugs, holding immense promise for cancer therapy and other chronic diseases where precision and controlled release are essential (Negut et al., 2023)(Kotta et al., 2022) [Fig 2].

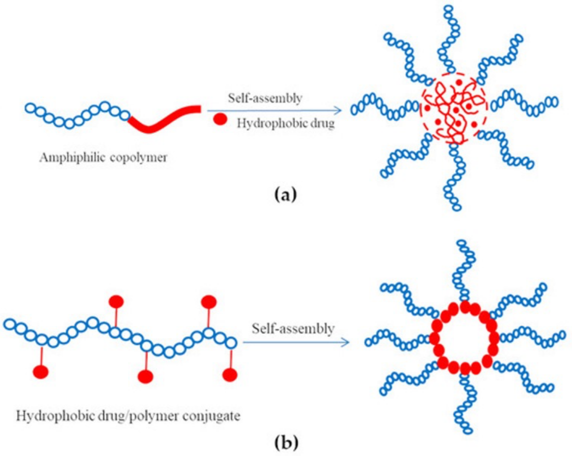

Figure 3: Schematic representation for the preparation of micellar drug delivery systems (DDS) by self-assembly; (a) physical drug entrapment; (b) self-assembly of drug/polymer conjugate formed by chemical or polyionic conjugation

Dendrimers:

Dendrimers were highly branched, monodisperse macromolecules that possessed a well-defined architecture with a central core, interior layers, and surface functional groups (J. Wang et al., 2022). Their nanoscale size and tunable surface make them suitable for controlled Drug delivery applications. In Transdermal drug delivery were used to increase the solubility and skin permeability of nonsteroidal anti-inflammatory drugs (NSAIDs). Ketoprofen, Diflunisal, and Indomethacin demonstrated improved absorption and bioavailability when complexed with PAMAM dendrimers. The dendrimer–drug conjugates allowed enhanced drug penetration through the stratum corneum and extended drug retention in dermal tissues (J. Wang et al., 2022)(Fadaei et al., 2025).

In Oral delivery, dendrimers were shown to improve the dissolution and stability of poorly soluble drugs. They acted as solubilizing agents and controlled-release carriers, which maintained steady plasma levels and reduced dosing frequency (Naji et al., 2022). For instance, conjugation of hydrophobic drugs to PAMAM dendrimers decreased cytotoxicity and improved gastrointestinal transport, suggesting their value for oral formulations (Naji et al., 2022)(Fadaei et al., 2025).

In nasal drug delivery, dendrimers were employed as carriers for small interfering RNA (siRNA) targeting brain tissues. Arginine-modified dendrimers formed nanosized complexes that enhanced nasal mucosal absorption and successfully delivered siRNA across the olfactory route. This resulted in significant suppression of high mobility group box 1 (HMGB1) protein expression and provided neuroprotection in experimental stroke models (Naji et al., 2022).

In central nervous system (CNS) therapy, dendrimers improved the permeability of therapeutic molecules across the blood–brain barrier. Drug-loaded dendrimers maintained stable plasma concentrations, prolonged half-life, and minimized side effects through targeted delivery. In addition, dendrimer-based platforms were investigated for anticancer, protein, and peptide delivery, where they efficiently encapsulated doxorubicin, methotrexate, and biologically active peptides, enhancing their solubility and tumor-specific accumulation (Naji et al., 2022)(J. Wang et al., 2022).

Nanogels:

Vaginal Drug Delivery Using Nanogels:

The nanostructured gels were also studied for delivering antibacterial and antimicrobial drugs in the management of several vaginal infections. Infected symptoms of nanogel formulations were decreased while minimizing vaginal discomfort and abnormal secretion (S et al., 2024). The nanogel formulation successfully relieved infection, concomitant symptoms and lessened vaginal discomfort and abnormal secretions. owing to their controlled and localized release nature, these systems had previously been assessed for the possibility of treating particular sexual health complications. the application of antiretroviral drug-loaded nanogels to reduce the risk of HIV transmission in women (S et al., 2024).

For instance, hydroxypropyl methylcellulose (HPMC K15M) was treated in a two-step desolvation process to produce gelatin-based nanoparticles with encapsulated tenofovir, a formulation researched for HIV prophylaxis. The nanogel served as a bioadhesive polymer and a gelling matrix and provided better mucosal adhesion and increased membrane permeability. The last formulation showed better drug retention and distribution in vaginal tissues, indicating its capacity as an efficient platform for localized antiretroviral treatment and controlled vaginal drug delivery (Suhail et al., 2019)(S et al., 2024).

Transdermal Drug Delivery Using Nanogels:

Transdermal drug delivery has several advantages over conventional administration routes, including the avoidance of first-pass metabolism, improved patient compliance, maintenance of steady plasma drug levels, and enhanced therapeutic efficacy. Numerous strategies have been developed to facilitate drug absorption through the skin, particularly via nanogel-based topical formulations, which enable efficient delivery of active pharmaceutical ingredients to the stratum corneum (S et al., 2024).

One notable example involved the transdermal delivery of aceclofenac, a non-steroidal anti-inflammatory drug (NSAID) commonly administered orally. Although effective, oral administration of aceclofenac had been associated with gastrointestinal side effects such as ulcers and gastric bleeding. They used an emulsion-based solvent diffusion technique to examine a nanogel formulation for aceclofenac, which involved incorporating an aceclofenac emulsion into a gel matrix, in order to get around these issues (S et al., 2024). The resulting nanogel exhibited superior stability, enhanced skin permeability, and improved drug release compared to conventional formulations. This system had demonstrated potential as a safer and more efficient approach for transdermal aceclofenac delivery, effectively minimizing gastrointestinal complications while maintaining therapeutic efficacy (Vashist et al., 2024)(S et al., 2024)(Delgado-Pujol et al., 2025).

Hyaluronic Acid:

Drug Delivery Systems for Solid Tumors:

Hyaluronic acid (HA)–based delivery systems have been widely used for drug delivery of their biocompatibility, biodegradability, and receptor-specific targeting ability (Pashkina et al., 2025). It functioned both as a structural component of the carrier and as a targeting ligand, binding effectively to receptors such as CD44, which were overexpressed on many tumor cells. This interaction enabled site-specific accumulation of drugs within cancerous tissues. A well-known Hyaluronic acid –paclitaxel conjugate, Oncofid-P, had entered clinical trials for bladder carcinoma, highlighting the translational potential of such systems. Hyaluronic acid could be chemically modified to produce multifunctional nanocarriers with improved solubility, stability, and controlled release properties (Pashkina et al., 2025). These systems enhanced bioavailability while minimizing first-pass metabolism. When combined with other materials, Hyaluronic acid maintained its targeting ability and introduced additional features, such as responsiveness to the tumor microenvironment. Supramolecular structures integrating HA and macrocyclic frameworks had shown promise for site-specific chemotherapy (Pashkina et al., 2025)(Fu et al., 2023).

Table 1: Clinical trials of HA-based drug delivery systems.

Drug Delivery System	**Tumor**	**ID Number**
Oncofid-P (paclitaxel–hyaluronic acid conjugate)	Bladder Carcinoma in Situ	NCT04798703 NCT05024773
Oncofid-P (paclitaxel–hyaluronic acid conjugate)	Non-Invasive Papillary Carcinoma of Bladder	NCT04661826
FOLFIRI versus FOLF(HA)iri (the FOLFIRI regimen with the “HA-Irinotecan”) regimen	Metastatic Colorectal Cancer	NCT01290783

Drug Delivery Systems for Hematological Malignancies:

Hematological malignancies originate from hematopoietic or lymphatic tissues and require maintaining therapeutic drug concentrations within the bone marrow. Conventional chemotherapy required high doses or frequent administration, which often resulted in significant systemic toxicity and side effects. Moreover, the bone marrow microenvironment contained tumor stem cells that were resistant to chemotherapy, contributing to treatment refractoriness and disease relapse (Pashkina et al., 2025).

CD44, a major receptor for hyaluronic acid (HA), was highly expressed in several hematological malignancies. his receptor had played a critical role in disease progression by promoting cell survival, apoptotic resistance, invasion, and leukemia cell homing within the bone marrow (Pashkina et al., 2025)(Salari et al., 2021). Moreover, CD44 receptors were also expressed on normal cells, particularly in the bloodstream, which reduced targeting precision and increased off-target effects. Dense tumor matrices further restricted drug penetration and distribution within tissues (Pashkina et al., 2025).

In order to enable dual targeting and siRNA loading for gene silencing, researchers created HA-coated nanoparticles for non-Hodgkin's lymphoma. The HA shell was covalently linked with anti-CD20 antibodies. Both in vitro and in vivo, these approaches suppressed tumor growth and triggered apoptosis. Selectivity against cancerous cells was further enhanced by a triple-targeted HA nanoparticle that included two antibodies (Pashkina et al., 2025). Similarly, in xenograft studies, doxorubicin-loaded HA nanoparticles cross-linked with lipoic acid (LACHA–DOX) demonstrated strong suppression of both acute myeloid leukemia (AML-2) and multiple myeloma (LP-1). In CD44-positive animals, other HA nanocarriers, including duvelisib-loaded and silver-based nanoparticles, also showed effectiveness by increasing the production of reactive oxygen species (ROS) and encouraging tumor cell death (Pashkina et al., 2025)(Fu et al., 2023).

Albumin-Bound Nanoparticles:

Albumin-bound nanoparticles had emerged as a leading platform for targeted drug delivery due to their high biocompatibility, structural versatility, and established clinical safety profile (Meng et al., 2022). Albumin, an abundant plasma protein, possesses exceptional ligand-binding capacity, broad tissue distribution, and a prolonged circulation half-life, making it a suitable carrier for diverse therapeutic molecules. The Albumin nanoparticles were primarily attributed to their functional groups, which allowed facile surface modification and binding of both hydrophilic and hydrophobic drugs(Meng et al., 2022). The most widely used albumin is human serum albumin (HSA) and bovine serum albumin (BSA), with HSA offering superior biocompatibility and reduced immunogenicity (Qu et al., 2024).

Albumin nanoparticles had been modified for targeted and controlled drug release. Passive targeting was improved through polyethylene glycol (PEG) coating, which prolonged systemic circulation and enhanced tumor accumulation. Active targeting was achieved by coupling ligands such as folic acid or monoclonal antibodies, enabling receptor-mediated uptake by tumor cells or inflamed tissues(Qu et al., 2024). Preclinical and clinical studies consistently supported the efficacy of albumin nanoparticles in improving therapeutic index, reducing systemic toxicity, and enabling site-specific delivery of antitumor and anti-inflammatory agents. Abraxane and Fyarro have been approved for targeted cancer therapy to expand the application of albumin-based carriers in autoimmune, inflammatory, and neurological disorders. This is a clinically proven and highly adaptable platform for targeted and controlled drug delivery (Qu et al., 2024).

Solid Lipid Nanoparticles (SLNs):

Hydrophilic Drugs on Solid Lipid Nanoparticles (SLNs):

Hydrophilic drugs had exhibited poor delivery, low intracellular uptake delivery, degradation, and rapid clearance, which collectively resulted in reduced bioavailability and limited therapeutic efficacy (Mirchandani et al., 2021). To avoid these limitations, solid lipid nanoparticles (SLNs) have been developed as promising carriers because of their biocompatibility, capacity to enhance stability, and potential for controlled drug release. However, the SLNs had remained challenging due to their weak affinity for the lipid matrix, leading to drug leakage and low entrapment efficiency (Mirchandani et al., 2021).

Several strategies had been worked to improve drug loading, including double emulsification (w/o/w), microemulsion template, and solvent diffusion methods. With the addition of drug modification, such as hydrophobic ion pairing (HIP), drug–polymer conjugation, and lipophilic prodrug formation, has been applied to increase lipid compatibility and encapsulation efficiency (Mirchandani et al., 2021). These techniques had 40% for insulin approximately and then it reached over 90% for insulin and cisplatin. Among these, HIP and polymer conjugation have proven particularly effective for stable encapsulation and sustained drug release (Mirchandani et al., 2021).

Table 2: List of hydrophilic drug-loaded SLNs prepared by either method modification or drug modification.

S. No.	Hydrophilic drug	Methods	Route of administration/purpose of study	Entrapment efficiency(%)
1.	Ampicillin	Solvent evaporation	Increase antibacterial activity	77
2.	Amikacin	Hot homogenization	Improved efficacy at lower doses	60-86
3.	Ascorbic Acid	Hot homogenization	Enhanced cellular uptake	90
4.	BACE 1-siRNA	Double emulsion	Increase permeation	-
5.	Calcitonin	Solvent evaporation	Oral	90

SOLID LIPID NANOPARTICLES (SLN) FOR BRAIN DRUG DELIVERY:

Solid lipid nanoparticles (SLNs) have been promising carriers for delivering anticancer drugs through the oral route. The inclusion of the SLNs for Brain drug delivery is to improve various issues like poor solubility, low intestinal absorption, and rapid breakdown in the body. SLNs helped to overcome these issues because they protected the drug, improved its absorption, and allowed controlled release at the target site (Satapathy et al., 2021).

In oral cancer, it played a significant role in improving the performance of anticancer agents. They carried the drugs safely through the digestive system and helped more of the medicine reach the bloodstream and tumor tissues. Since the lipid materials used in SLNs were biocompatible, they reduced the toxic effects that usually came with chemotherapy drugs (Satapathy et al., 2021). This feature was especially useful because many traditional anticancer drugs harmed healthy tissues while attacking cancer cells. In later research, the SLNs could increase the bioavailability of anticancer drugs by preventing them from breaking down in the stomach and enhancing their movement through the intestinal wall (Satapathy et al., 2021). The small size of SLNs also allowed them to pass more easily into cancer cells. Moreover, drugs such as curcumin, docetaxel, and doxorubicin showed better oral absorption and stronger anticancer effects when formulated with SLNs compared to conventional methods. Some surface-modified SLNs, like those coated with polyethylene glycol or folic acid, targeted tumor cells more directly and reduced damage to normal cells (Satapathy et al., 2021).

SOLID LIPID NANOPARTICLES (SLN) for Prostate Cancer:

Prostate cancer has been recognized as one of the most common and serious cancers in men, especially in developed countries (Mendoza-Muñoz et al., 2021). This has increased over the last decade because of the complex and variable nature of tumors and the difficulty in targeting cancer cells with conventional therapies. Solid lipid nanoparticles (SLNs) are the potential solution to improve the treatment of prostate cancer (Akanda et al., 2023).

SLNs had several benefits, including the use of safe and biocompatible materials, good physical stability, and the elimination of toxic organic solvents during preparation. These nanoparticles were capable of accumulating more effectively in tumor tissues through the enhanced permeability and retention (EPR) effect, which allowed passive targeting (Mendoza-Muñoz et al., 2021). When specific ligands were attached to their surface, SLNs also achieved active targeting through receptor-mediated endocytosis, improving drug delivery to cancer cells. The anticancer properties of ellagic acid, a natural polyphenol, became more effective against prostate cancer when encapsulated in SLNs. The ellagic acid-loaded SLNs inhibited the growth of PC3 prostate cancer cells with a lower IC50 value than the free drug, indicating stronger cytotoxic activity. This results in controlling prostate cancer cell growth (Akanda et al., 2023).

Gold Nanoparticles:

GNPs for nucleic acid delivery:

Gold nanoparticles (GNPs) have been utilized as effective carriers of nucleic acids for treating various diseases, such as cancer, acquired immunodeficiency syndrome, and neurological disorders (Khlebtsov et al., 2011). When nucleic acids were introduced into the body, they encountered numerous biological barriers that hindered them from reaching their desired cells. Both non-viral and viral nanocarriers, such as GNPs, have assisted in crossing these barriers and facilitated intracellular delivery of genetic material like antisense oligonucleotides and aptamers. GNPs have been commonly applied in oncology for gene therapy due to their potential for safe and efficient delivery of nucleic acids. One such breakthrough was RNA interference (RNAi), a biological process by which small double-stranded RNA molecules repress certain genes following transcription. Short interfering RNAs (siRNAs) were very promising for cancer and viral infection therapies. But their instability and inability to reach target tissues hampered their utility. GNPs alleviated many of these issues by stabilizing siRNA against degradation, enhancing its targeting in target tissues, and suppressing toxicity (Ramadan et al., 2025). Their shape, size, and optical characteristics might also be modified for improved performance. Various GNPs, like nanospheres, nanocages, and nanorods, have exhibited differential loading and release capabilities for siRNA. Nanospheres contained a higher amount of siRNA, whereas nanorods released it more effectively. All the forms were observed to penetrate cells well and repress gene expression. Advanced systems that integrated small-molecule therapeutics and siRNA within one GNP-based platform showed robust tumor suppression, validating the potential of this technology in cancer treatment (Khlebtsov et al., 2011).

Apart from gene silencing, GNPs were also investigated for transporting genetic editing tools such as CRISPR/Cas9. The system enabled specific gene modification and had vast potential in cancer therapy(Ramadan et al., 2025). Yet, safe and effective delivery of the components of CRISPR was a significant challenge. GNP-based carriers offered a potential solution by ensuring stability, target transport, and controlled delivery of genetic materials (Ramadan et al., 2025).

In addition, GNPs were applied to create nucleic acid-based vaccines, which depended on the use of DNA or mRNA for the generation of target proteins to initiate immune responses (Khlebtsov et al., 2011). The vaccines were beneficial because they could be designed rapidly, were capable of being adapted to evolving pathogens, and could induce cellular and humoral immunity. GNPs served as carriers due to their roles of stabilizing sensitive nucleic acids as well as facilitating multi-molecule vaccine delivery at the same time (Khlebtsov et al., 2011).

GNPs for antibiotic delivery:

Gold nanoparticles (GNPs) used as carriers for anticancer drugs; the small particles have the potential to accumulate in tumors through leaky blood vessels under the enhanced permeation and retention (EPR) effect. This delivered the drugs directly to cancer locations while minimizing damage to healthy tissue (Khlebtsov et al., 2011)(Lopes-Nunes et al., 2021). For instance, they conjugated paclitaxel, a compound that inhibits the division of cancer cells, to GNPs, and mouse tests revealed it accumulated more in tumors and killed cancer cells more efficiently than the drug itself. Likewise, docetaxel conjugated to GNPs was 2.5 times more potent against breast cancer cells (Khlebtsov et al., 2011). Methotrexate, another anticancer cell-killer, when linked with GNPs, penetrated tumor cells earlier and in greater quantities, increasing its efficacy against many cancers such as lung and bladder cancers, and even against arthritis in animals (Khlebtsov et al., 2011). Daunorubicin and 6-mercaptopurine, both employed to treat leukemia, exhibited enhanced effects when delivered via GNPs, as they targeted resistant cells and enhanced toxicity to tumors. Gemcitabine with GNPs and an antibody named cetuximab reduced pancreatic cancer growth in mice by targeting specific growth receptors (Khlebtsov et al., 2011)(Huang et al., 2023).

Other antibodies, such as panitumumab and trastuzumab, when daunorubicin and 6-mercaptopurine, both employed to treat leukemia, exhibited enhanced effects when delivered via GNPs, as they targeted resistant cells and enhanced toxicity to tumors (Lopes-Nunes et al., 2021). Gemcitabine with GNPs and an antibody named cetuximab reduced pancreatic cancer growth in mice by targeting specific growth receptors. combined with GNPs and drugs, enhanced targeting and minimized side effects (Khlebtsov et al., 2011).

5-Fluorouracil, a widely used chemo drug, was released slowly from GNPs under UV light and doubled its potency against breast cancer cells. Kahalalide F, a peptide drug, entered cells more effectively with GNPs, enhancing its lethal effect. Tamoxifen for breast cancer was made 2.7 times more effective upon conjugation (Huang et al., 2023). Prospidin and vincristine, conjugated to GNPs, increased cell death in tumors by inhibiting the cell cycle. Doxorubicin, a potent antibiotic-like chemotherapy, administered through different GNP structures such as spheres, rods, and shells, penetrated into cell nuclei and inflicted up to four times more damage on lung, melanoma, and brain cancer cells; it was even used in clinical trials for liver and pancreatic cancer (Khlebtsov et al., 2011)(Lopes-Nunes et al., 2021).

Oxaliplatin and cisplatin, platinum-based pharmaceuticals, enhanced their penetration into lung and colon cancer cells with GNPs, increasing the level of reactive oxygen and initiating cell suicide. Bortezomib against pancreatic cancer entered cells faster with GNPs, and mitoxantrone on star-shaped GNPs targeted lung tumors well. Epirubicin, sunitinib, alendronate, dasatinib, etoposide, quinacrine, letrozole, and pemetrexed all had greater anti-tumor effects when GNP-bound, typically by increasing apoptosis or inhibiting blood flow to tumors, merging drugs such as cisplatin with doxorubicin on GNPs formed "triple" treatments that targeted cancers more intensely at regions of lower dosage. Aside from chemo, GNPs transported proteins such as tumor necrosis factor to reduce tumors in mice without accumulating in the liver, and enzymes that deprived cancers of essential nutrients(Khlebtsov et al., 2011).In immunotherapy, GNPs are used to transport antigens and blockers, initiating immune responses against tumors, with some vaccines progressing to initial human trials. In general, these reports underscored how GNPs transformed anticancer drugs to become less toxic and more potent by enhancing drug stability, targeting, and release (Khlebtsov et al., 2011)(Huang et al., 2023).

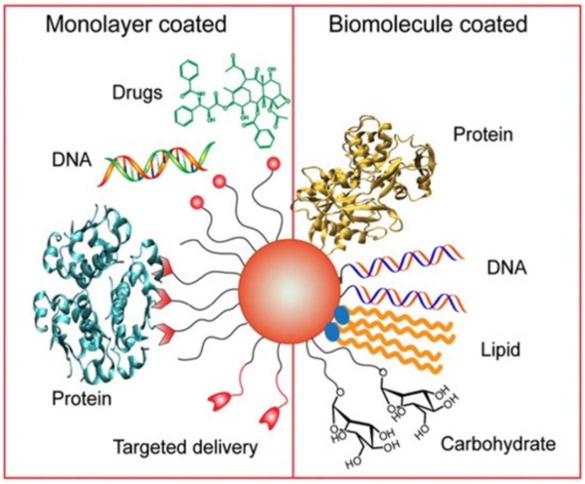

Figure 4: Scheme for the two GNP surface structures commonly used in delivery applications(Ramadan et al., 2025).

Iron Oxide Nanoparticles:

Magnetically-guided drug delivery:

Magnetically guided drug delivery has been developed as an advanced method to transport therapeutic agents directly to diseased tissues using magnetic nanoparticles, mainly iron oxide–based systems. The nanoparticles had been engineered to be sensitive to external magnetic fields, allowing researchers to control the direction and deposition of drugs to the target (Stanicki et al., 2022).

Iron oxide nanoparticles have been the most widely used magnetic carriers due to their high magnetic response, stability, and biocompatibility. Their surfaces were typically coated with polymers, lipids, or other biocompatible materials to enhance drug loading, stability, and blood circulation time (Vangijzegem et al., 2019). Drugs were encapsulated within or chemically attached to the surface of these nanoparticles. Magnetic guidance utilization aided in bypassing biological barriers, decreasing systemic toxicity, and enhancing therapeutic efficiency (Stanicki et al., 2022).

The recent studies showed that magnetically guided systems increased anticancer drug targeting to cancer tissues. This significantly raised the concentration of drugs at the site of disease and reduced exposure to normal organs (Vangijzegem et al., 2019). Besides, these nanoparticles were employed in hyperthermia therapy, where localized hyperthermia under a magnetic field killed cancer cells and augmented chemotherapy effectiveness. It had integrated imaging, targeted therapy, and controlled heating into one platform, offering an efficient, safe, and non-invasive treatment approach for diverse cancers and other localized diseases (Stanicki et al., 2022).

IONs-based targeted drug delivery in cancer theranostics:

Iron oxide nanoparticles (IONs) have been widely studied for targeted drug delivery and cancer theranostics because of their magnetic properties, biocompatibility, and ability to be tracked through imaging. IONs in cancer treatment have been employed to deliver chemotherapeutic drugs specifically to cancerous tissues. After being guided to the target site by an external magnet, the nanoparticles delivered the drugs in a controlled release(Estelrich et al., 2015). This localized administration was a way to boost drug concentration within the tumor site and reduce exposure to normal tissues. Moreover, IONs were used in hyperthermia therapy, in which alternating magnetic fields created heat to destroy cancer cells and synergized with chemotherapy or radiation (Qiao et al., 2023).

IONs also performed as diagnostic agents due to their excellent magnetic resonance contrast, enabling clinicians to track drug delivery and tumor response in real time. Integration of imaging and therapy in the same device rendered ION-based nanocarriers useful for individualized cancer treatment (Stanicki et al., 2022).

In all, ION-mediated targeted drug delivery has a versatile platform for cancer theranostics. Their capacity to integrate drug delivery, imaging, and hyperthermia resulted in an effective and multifunctional platform for enhancing the accuracy and efficiency of cancer treatment (Estelrich et al., 2015).

Mesoporous Silica Nanoparticles:

Mesoporous silica-based system for gene delivery:

Mesoporous silica nanoparticles (MSNs) were a promising leap in gene delivery, as they are large in surface area, pore size tunable, and surface functionalizable. MSNs were widely investigated as non-viral gene carriers in search of alternatives to viral vectors, which traditionally had safety and specificity issues. MSNs had a negative surface charge, lowering their interaction with the negatively charged nucleic acids (Santhamoorthy et al., 2025). To solve this, they altered silica nanoparticles to introduce positive charges by different means, including amination, metal cation charge, and cationic polymers like polyamidoamine (PAMAM), polyethyleneimine (PEI), and poly-L-lysine (PLL). The alterations promoted electrostatic interactions, enhancing the adsorption of genes and internalization by cells. Experiments proved that the extent of amination was proportional to DNA adsorption capacity and that PEI-coated MSNs had transfection efficiencies ranging from 70% in some cell lines. The proton sponge effect of PEI further facilitated endosomal escape, enhancing gene delivery rates(Santhamoorthy et al., 2025).

Multifunctional MSNs were engineered to co-deliver drugs, targeting ligands, and genes with imaging agents. The systems targeted multidrug resistance in cancer treatment by allowing for concurrent delivery of chemotherapeutics and gene silencing agents(Santhamoorthy et al., 2025). Targeting moieties, including mannose or antibodies, were attached to MSNs to target gene delivery to particular cell types and evade cellular uptake limitations. Magnetic nanoparticles and fluorescent markers were further incorporated to enable tracking, targeting, and imaging of delivery. mesoporous silica-based systems were the key to paving the way for gene delivery technology, providing reconfigurable, multifunctional platforms with high efficiency, safety, and potential for clinical use in the treatment of a wide range of diseases (Santhamoorthy et al., 2025).

Mesoporous silica-based system for cancer therapy:

Mesoporous silica nanoparticles (MSNs) have been widely investigated as an effective system for cancer therapy because of their unique structural and chemical properties. Their large surface area, adjustable pore size, and easy surface modification allowed them to carry a wide variety of anticancer agents and deliver them directly to tumor tissues. MSNs offered improved drug stability, controlled release, and better targeting compared to conventional drug delivery systems (Santhamoorthy et al., 2025).

Different Mesoporous silica nanoparticles are formulated to enhance treatment efficiency while minimizing damage to healthy tissues. These nanoparticles were functionalized with targeting ligands such as folic acid, peptides, or antibodies that specifically recognized receptors overexpressed on cancer cells (Khalbas et al., 2024). This targeted approach allowed higher drug accumulation in tumor sites through receptor-mediated uptake. Additionally, MSNs were engineered to release drugs in response to internal tumor conditions like acidic pH or enzyme activity, ensuring localized and sustained drug action (Santhamoorthy et al., 2025).

MSNs have a combination with other therapeutic approaches, i.e., photothermal and photodynamic therapy. With the incorporation of photosensitive or heat-producing agents, the nanoparticles induced localized heat or reactive oxygen species upon light or magnetic stimulation, which killed cancer cells more effectively. Dual or multi-functional MSNs incorporating chemotherapy, gene therapy, and imaging agents presented synergistic effects, showing enhanced tumor inhibition and less systemic toxicity (Santhamoorthy et al., 2025).

Preclinical tests proved that MSN-based drug carriers greatly improved the therapeutic index of anticancer agents such as doxorubicin, paclitaxel, and cisplatin. Because of their biocompatibility and stability in biological conditions, they were useable for extended periods (Santhamoorthy et al., 2025)(Khalbas et al., 2024).

Carbon Nanotubes:

Drug delivery targeted to the lymphatic system:

Magnetic iron oxide (Fe_3O_4) nanoparticles were adsorbed on the PAA-coated CNT surface through coprecipitation. The carboxyl groups of PAA helped to keep the magnetic nanoparticles stable and well-dispersed(Zhang et al., 2011).

Gemcitabine, a cancer chemotherapy agent, was loaded into this nanosystem by mixing it with the PAA-CNT-Fe_3O_4 composite for 24 hours, obtaining a drug-loading efficiency of around 62%. The CNTs after subcutaneous injection primarily collected in the surrounding lymph nodes and were not detected in other key organs like the liver, kidney, spleen, or lungs. This demonstrated that the system of CNT effectively targeted the drug to the lymphatic tissues(Zhang et al., 2011).

In the absence of such a nanocarrier, gemcitabine did not accumulate in lymph nodes. so magnetic drug delivery systems based on CNT offered an effective strategy for the delivery of drugs to lymphatic tissues, which was responsible for inhibiting or treating metastasis of cancer via the lymphatic routes(Zhang et al., 2011)(Tajabadi, 2025).

Carbon Nanotubes Improve Breast Cancer Therapy:

Carbon nanotubes (CNTs) have been found to improve breast cancer therapy by acting as efficient carriers for targeted drug delivery and therapeutic agents. Their unique mechanical strength, high surface area, and ability to be easily modified made them suitable for transporting drugs directly into cancer cells while minimizing harm to healthy tissues. Because CNTs were not immunogenic and showed low toxicity after surface modification, they offered a safer platform for breast cancer treatment (Zhang et al., 2011)(Achar et al., 2025).

They designed a number of CNT-based drug delivery systems for breast cancer. For instance, Singh et al. prepared paclitaxel-loaded multi-walled carbon nanotubes (MWCNTs) functionalized with thiamine and riboflavin to target specifically MCF-7 breast cancer cells. These formulations showed very high efficiency in cancer cell killing, exhibiting the potential of CNTs in targeted therapy. In the same vein, Al Faraj et al. designed doxorubicin-loaded single-walled CNTs (SWCNTs) for the treatment of metastatic tumors. With MRI imaging, they followed and verified the nanoparticles' deposit at cancerous places, which increased treatment accuracy (Achar et al., 2025).

CNTs were also utilized in photothermal and photodynamic treatments. Scientists conjugated monoclonal antibodies against HER2 and IGF1 receptors on breast cancer cells to SWCNTs, enabling targeted cell destruction when exposed to near-infrared (NIR) illumination. The selective heating destroyed the cancer cells without harming adjacent tissues (Zhang et al., 2011).

CNTs were also used in photothermal and photodynamic therapies. They attached monoclonal antibodies specific to HER2 and IGF1 receptors on breast cancer cells to SWCNTs, allowing targeted destruction of tumor cells when exposed to near-infrared (NIR) light. This selective heating helped eliminate cancer cells without damaging surrounding tissues (Achar et al., 2025).

Quantum Dots:

Quantum dots had appeared as a versatile and multifunctional platform for Targeted drug delivery due to their tunable optical properties, high surface-to-volume ratio, and excellent biocompatibility [Fig 4]. Their inherent fluorescence and quantum confinement make them suitable nanosystems that can perform dual roles—as drug carriers and imaging probes (Hamidu et al., 2023). The nanoscale size of QDs enables passive tumor tissue accumulation via the EPR effect, and their surface may be engineered with ligands like polyethylene glycol (PEG), peptides, antibodies, or folic acid for active, receptor-mediated targeting(Hamidu et al., 2023)[Fig 5].

Surface modification is an essential aspect of QD-based delivery systems. Functional ligands enable covalent or electrostatic attachment of therapeutic molecules, creating stable nano-drug conjugates with the ability to monitor intracellular localization through fluorescence. For example, PEGylated ZnO and graphene QDs loaded with doxorubicin or platinum-based anticancer drugs have been shown to have increased cellular uptake, pH-responsive release, and enhanced cytotoxicity against cancer cells with reduced systemic toxicity (Hamidu et al., 2023). In the same way, polymer matrices like polylactic acid (PLA) and carboxymethyl cellulose have been employed for encapsulating QDs, allowing controlled and sustained drug release in acidic tumor microenvironments. Due to heavy metal elements like cadmium and indium, the toxicity continued to be a major limitation. Strategies for synthesizing metal-free or silica-capped QDs have provided enhanced biocompatibility and minimized ion leaching. Optimization of surface coatings, biodegradability, and excretion routes continues to be essential for clinical translation (Hamidu et al., 2023).

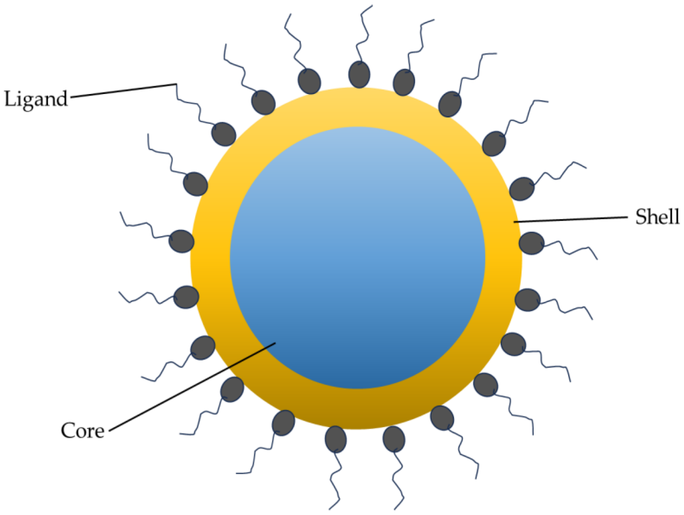

Figure 5: Structure of a QD showing the core/shell/ligand (Hamidu et al., 2023)

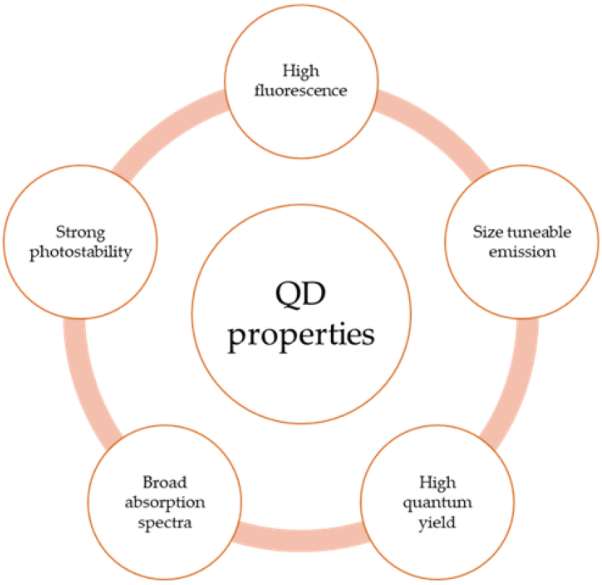

Figure 6: Diagram showing some optical properties of QDs(Hamidu et al., 2023).

Chitosan Nanoparticles:

Ocular Drug Delivery:

Chitosan nanoparticles were used as drug carriers for ocular drug delivery since they enhanced the drug's contact time with the eye surface and minimized repeated dosing. Classic eye drops possessed low bioavailability as a result of tear drainage and blinking, yet chitosan nanoparticles overcame these obstacles by virtue of their mucoadhesive and permeation-facilitating capacities(Obeidat et al., 2025). Their positive charge facilitated strong interaction with the negatively charged mucin layer, which prolonged drug residence on the corneal surface. Chitosan possessed good film-forming, biodegradable, and non-irritant behavior, rendering it adequate for sensitive ocular tissues (Obeidat et al., 2025).

Chitosan nanoparticle formulated with multiple drugs like cyclosporine A, indomethacin, pilocarpine, and fluconazole. These products delivered sustained and controlled drug delivery, enhanced the solubility of poorly soluble drugs, and increased therapeutic efficacy against standard eye drops. Trimethyl chitosan-modified chitosan systems also improved mucoadhesion and permeability (Obeidat et al., 2025).

Oral Drug Delivery:

Oral drug delivery in chitosan nanoparticles used for enhanced absorption and stability of drugs in the gastrointestinal tract by these nanoparticles. Several drugs suffered from issues like poor solubility, instability in stomach acid, and poor intestinal permeability, thus restricting their efficacy. Chitosan was biodegradable, biocompatible, and cationic in nature and interacted with negatively charged mucosal surfaces and facilitated drug transit across intestinal membranes more effectively (Stefanache et al., 2025). They employed chitosan nanoparticles for the delivery of hydrophilic and hydrophobic drugs with improved control over drug release as well as for protection of sensitive molecules such as peptides and proteins from degradation (Obeidat et al., 2025). Modified types like trimethyl chitosan and thiolated chitosan further increased permeability and mucoadhesion, resulting in increased oral bioavailability drug absorption was enhanced and the therapeutic duration prolonged when compared to standard oral tablets or suspensions by chitosan-based formulations. chitosan nanoparticles had an effective and safe platform for enhancing oral drug delivery through ensuring improved stability, absorption, and controlled release of drugs (Dash et al., 2025)(Stefanache et al., 2025).

Extracellular Vesicles:

Targeted drug delivery via extracellular vesicle (EV) is created to enhance the accuracy and therapeutic efficacy of cancer therapy(Verma et al., 2025). Since tumors presented with complicated microenvironments and cell heterogeneity, extracellular vesicles needed to be modified so that they could target cancer cells effectively. For better improvement, 4 main strategies are followed they are surface modification, selection of cell sources, biomaterial integration, and targeting assistance from magnetic nanoparticles (Verma et al., 2025).

In surface engineering, chemically modified EV membranes are used to conjugate targeting ligands like folate, ephrin-B2, or RGD peptides. These ligands selectively bound to receptors that are overexpressed on cancer cells, which improved the EV uptake and drug delivery. by the time olate exhibited high affinity to folate receptors expressed in ovarian cancer, whereas EVs modified by RGD targeted integrin receptors. Certain EVs were designed with antibodies such as anti-EGFR or HER2 for highly targeted tumor targeting and off-target toxicity reduction(Langellotto et al., 2024).

The cell source selection approach on the selection of donor cells with inherent tumor properties. Mesenchymal stem cell (MSC)-derived extracellular vesicles (EVs) were taken up by tumor tissues in an efficient manner owing to their intrinsic tropism and thus proved to be good carriers for chemotherapeutic agents or photodynamic therapy agents(Langellotto et al., 2024)(Herrmann et al., 2021). Immune cell-derived EVs, including natural killer cells, T cells, and dendritic cell-derived EVs, transferred cytotoxic proteins as well as immune-stimulating molecules, with a beneficial effect on suppressing tumor growth and immunomodulation.

Integration with biomaterials such as hydrogels and 3D-printed scaffolds offered protection and controlled release of EVs at desired sites. Hydrogels assisted in enhancing EV retention and avoiding premature degradation, providing better therapeutic benefits. Some 3D scaffolds were even engineered to trap metastatic cancer cells and transform extensive metastasis into a local, removable disorder(Rawat et al., 2025).

Lastly, magnetic nanoparticle-based targeting employed iron oxide or other magnetic nanoparticles in EVs. By external magnetic field application, the EVs were specifically targeted to the tumor sites, which improved drug loading and reduced systemic toxicity(Rawat et al., 2025).

Conclusion:

Nanocarrier-based drug delivery represents a transformative leap toward intelligent and patient-specific therapy. By manipulating materials at the nanoscale, these systems achieve unprecedented control over drug transport, release kinetics, and site-specific action. The diversity of nanocarriers from liposomal vesicles to polymeric scaffolds and smart nanogels illustrates the versatility of nanotechnology in addressing complex pharmacological challenges. However, while preclinical results are promising, large-scale clinical translation still demands advancements in biocompatibility, reproducibility, and regulatory standardization. Future innovations will likely integrate nanocarriers with artificial intelligence, biosensing, and genomic tools to create adaptive "smart drug systems" capable of dynamic response to biological cues. Ultimately, nanocarriers stand at the forefront of a paradigm shift, transforming drug delivery from a passive process into a programmable, targeted, and efficient therapeutic technology poised to redefine modern medicine.

Conflict of Interest:
There is no conflict of interest.
Funding:
No funding received.

REFERENCES:

1. Achar, A., Myers, R., & Ghosh, C. (2025). Carbon nanotubes in brain targeted drug delivery: A comprehensive review. *Results in Chemistry*, *15*(12), 102206. https://doi.org/10.3390/biomedicines9121834
2. Akanda, M., Mithu, M. S. H., & Douroumis, D. (2023). Solid lipid nanoparticles: An effective lipid-based technology for cancer treatment. *Journal of Drug Delivery Science and Technology*, *86*, 104709. https://doi.org/10.1016/j.jddst.2023.104709
3. Atanase, L. I. (2021). Micellar Drug Delivery Systems Based on Natural Biopolymers. *Polymers 2021, Vol. 13, 13*(3), 1–33. https://doi.org/10.3390/polym13030477
4. Begines, B., Ortiz, T., Pérez-Aranda, M., Martínez, G., Merinero, M., Argüelles-Arias, F., & Alcudia, A. (2020). Polymeric Nanoparticles for Drug Delivery: Recent Developments and Future Prospects. *Nanomaterials*, *10*(7), 1403. https://doi.org/10.3390/nano10071403
5. Castro, K. C. de, Costa, J. M., & Campos, M. G. N. (2022). Drug-loaded polymeric nanoparticles: a review. *International Journal of Polymeric Materials and Polymeric Biomaterials*, *71*(1), 1–13. https://doi.org/10.1080/00914037.2020.1798436
6. Dash, B. S., Lai, Y. C., & Chen, J. P. (2025). Folic Acid-Conjugated Magnetic Oleoyl-Chitosan Nanoparticles for Controlled Release of Doxorubicin in Cancer Therapy. *Nanomaterials 2025, Vol. 15, Page 415*, *15*(6), 415. https://doi.org/10.3390/nano15060415
7. Delgado-Pujol, E. J., Martínez, G., Casado-Jurado, D., Vázquez, J., León-Barberena, J., Rodríguez-Lucena, D., Torres, Y., Alcudia, A., & Begines, B. (2025). Hydrogels and Nanogels: Pioneering the Future of Advanced Drug Delivery Systems. *Pharmaceutics 2025, Vol. 17, Page 215*, *17*(2), 215. https://doi.org/10.3390/pharmaceutics17020215
8. Estelrich, J., Escribano, E., Queralt, J., & Busquets, M. A. (2015). Iron Oxide Nanoparticles for Magnetically-Guided and Magnetically-Responsive Drug Delivery. *International Journal of Molecular Sciences*, *16*(4), 8070. https://doi.org/10.3390/ijms16048070
9. Fadaei, M. R., Fadaei, M. S., Kheirieh, A. E., Hatami, H., Rahmanian-Devin, P., Tayebi-Khorrami, V., Fathabadi, M. F., Baradaran Rahimi, V., & Askari, V. R. (2025). Overview of dendrimers as promising drug delivery systems with insight into anticancer and anti-microbial applications. *International Journal of Pharmaceutics: X*, *10*. https://doi.org/10.1016/j.ijpx.2025.100390
10. Fu, C. P., Cai, X. Y., Chen, S. L., Yu, H. W., Fang, Y., Feng, X. C., Zhang, L. M., & Li, C. Y. (2023). Hyaluronic Acid-Based Nanocarriers for Anticancer Drug Delivery. *Polymers*, *15*(10). https://doi.org/10.3390/polym15102317
11. Gong, J., Chen, M., Zheng, Y., Wang, S., & Wang, Y. (2012). Polymeric micelles drug delivery system in oncology. *Journal of Controlled Release*, *159*(3), 312–323. https://doi.org/10.1016/j.jconrel.2011.12.012
12. Guimarães, D., Cavaco-Paulo, A., & Nogueira, E. (2021). Design of liposomes as drug delivery system for therapeutic applications. *International Journal of Pharmaceutics*, *601*. https://doi.org/10.1016/j.ijpharm.2021.120571
13. Hamidu, A., Pitt, W. G., & Husseini, G. A. (2023). Recent Breakthroughs in Using Quantum Dots for Cancer Imaging and Drug Delivery Purposes. *Nanomaterials 2023, Vol. 13*, *13*(18). https://doi.org/10.3390/nano13182566
14. Herrmann, I. K., Wood, M. J. A., & Fuhrmann, G. (2021). Extracellular vesicles as a next-generation drug delivery platform. *Nature Nanotechnology*, *16*(7), 748–759. https://doi.org/10.1038/s41565-021-00931-2

15. Huang, H., Liu, R., Yang, J., Dai, J., Fan, S., Pi, J., Wei, Y., & Guo, X. (2023). Gold Nanoparticles: Construction for Drug Delivery and Application in Cancer Immunotherapy. *Pharmaceutics 2023, Vol. 15, 15*(7). https://doi.org/10.3390/pharmaceutics15071868
16. Khalbas, A. H., Albayati, T. M., Ali, N. S., & Salih, I. K. (2024). Drug loading methods and kinetic release models using of mesoporous silica nanoparticles as a drug delivery system: A review. *South African Journal of Chemical Engineering*, *50*(19), 261–280. https://doi.org/10.1016/j.sajce.2024.08.013
17. Khlebtsov, N., & Dykmana, L. (2011). Biodistribution and toxicity of engineered gold nanoparticles: a review of in vitro and in vivo studies. *Chemical Society Reviews*, *40*(3), 1647–1671. https://doi.org/10.1039/c0cs00018c
18. Kotta, S., Aldawsari, H. M., Badr-Eldin, S. M., Nair, A. B., & YT, K. (2022). Progress in Polymeric Micelles for Drug Delivery Applications. *Pharmaceutics*, *14*(8). https://doi.org/10.3390/pharmaceutics14081636
19. Langellotto, M. D., Rassu, G., Serri, C., Demartis, S., Giunchedi, P., & Gavini, E. (2024). Plant-derived extracellular vesicles: a synergetic combination of a drug delivery system and a source of natural bioactive compounds. *Drug Delivery and Translational Research*, *15*(3), 831–845. https://doi.org/10.1007/s13346-024-01698-4
20. Liu, S., Tan, B., Wang, F., & Yu, Y. (2025). Applications of polymeric nanoparticles in drug delivery for glioblastoma. *Frontiers in Pharmacology*, *15*. https://doi.org/10.3389/fphar.2024.1519479
21. Lopes-Nunes, J., Agonia, A. S., Rosado, T., Gallardo, E., Palmeira-De-oliveira, R., Palmeira-De-oliveira, A., Martinez-De-oliveira, J., Fonseca-Moutinho, J., Campello, M. P. C., Paiva, A., Paulo, A., Vulgamott, A., Ellignton, A. D., Oliveira, P. A., & Cruz, C. (2021). Aptamer-functionalized gold nanoparticles for drug delivery to gynecological carcinoma cells. *Cancers*, *13*(16), 4038. https://doi.org/10.3390/cancers13164038
22. Mendoza-Muñoz, N., Urbán-Morlán, Z., Leyva-Gómez, G., De La Luz Zambrano-Zaragoza, M., Piñón-Segundo, E., & Quintanar-Guerrero, D. (2021). Solid Lipid Nanoparticles: An Approach to Improve Oral Drug Delivery. *Journal of Pharmacy & Pharmaceutical Sciences : A Publication of the Canadian Society for Pharmaceutical Sciences, Societe Canadienne Des Sciences Pharmaceutiques*, *24*, 509–532. https://doi.org/10.18433/jpps31788
23. Meng, R., Zhu, H., Wang, Z., Hao, S., & Wang, B. (2022). Preparation of Drug-Loaded Albumin Nanoparticles and Its Application in Cancer Therapy. *Journal of Nanomaterials*, *2022*. https://doi.org/10.1155/2022/3052175
24. Mirchandani, Y., Patravale, V. B., & Brijesh, S. (2021). Solid lipid nanoparticles for hydrophilic drugs. *Journal of Controlled Release : Official Journal of the Controlled Release Society*, *335*, 457–464. https://doi.org/10.1016/j.jconrel.2021.05.032
25. Naji, G. H., Yousif Fareed, N., & Al-Zheery, W. H. (2022). Dendrimer as a Recent Drug Delivery System: An Overview. *Journal of Biomedicine and Biochemistry*, *1*(3), 57–69. https://doi.org/10.57238/jbb.2022.20109
26. Negut, I., & Bita, B. (2023). Polymeric Micellar Systems—A Special Emphasis on “Smart” Drug Delivery. *Pharmaceutics 2023, Vol. 15, Page 976*, *15*(3), 976. https://doi.org/10.3390/pharmaceutics15030976
27. Obeidat, W. M., & Lahlouh, I. K. (2025). Chitosan Nanoparticles: Approaches to Preparation, Key Properties, Drug Delivery Systems, and Developments in Therapeutic Efficacy. *AAPS PharmSciTech 2025 26:5*, *26*(5), 108-. https://doi.org/10.1208/s12249-025-03100-z
28. Pashkina, E., Bykova, M., Berishvili, M., Lazarev, Y., & Kozlov, V. (2025). Hyaluronic Acid-Based Drug Delivery Systems for Cancer Therapy. *Cells 2025, Vol. 14, Page 61*, *14*(2), 61. https://doi.org/10.3390/cells14020061
29. Qiao, R., Fu, C., Forgham, H., Javed, I., Huang, X., Zhu, J., Whittaker, A. K., & Davis, T. P. (2023). Magnetic iron oxide nanoparticles for brain imaging and drug delivery. *Advanced Drug Delivery Reviews*,

197. https://doi.org/10.1016/j.addr.2023.114822

30. Qu, N., Song, K., Ji, Y., Liu, M., Chen, L., Lee, R. J., & Teng, L. (2024). Albumin Nanoparticle-Based Drug Delivery Systems. *International Journal of Nanomedicine*, *19*, 6945–6980. https://doi.org/10.2147/IJN.S467876
31. Ramadan, A. E. hakim, Abdullah, H. D., Nabet, R. Y., Shehata, R. A., Gohar, M. H., Elmorsy, A. H., Elteray, N. A., Elseddiq, H. M., shreeda, D. A., Abd Almotaleb, E. A., Mohammed, E. H., Aldesouky, A. G., El Adlany, D. E., Ahmed, S. A., Maarouf, S. M., Galal, F. N., kiwan, M. E., Mohamed, M. M., Mohamed, N. A., … Kamal, I. (2025). Gold Nanoparticles in Drug Delivery Systems for Cancer Treatment: A Review. *Octahedron Drug Research*, *7*(1), 35–48. https://doi.org/10.21608/odr.2025.380813.1053
32. Rawat, S., Arora, S., Dhondale, M. R., Khadilkar, M., Kumar, S., & Agrawal, A. K. (2025). Stability Dynamics of Plant-Based Extracellular Vesicles Drug Delivery. *Journal of Xenobiotics 2025, Vol. 15, Page 55*, *15*(2), 55. https://doi.org/10.3390/jox15020055
33. S, F., Umashankar, M. S., Narayanasamy, D., Sirajudheen, F., Sr., M. S. U., & Narayanasamy, D. (2024). A Comprehensive Review of Nanogel-Based Drug Delivery Systems. *Cureus*, *16*(9). https://doi.org/10.7759/cureus.68633
34. Salari, N., Mansouri, K., Valipour, E., Abam, F., Jaymand, M., Rasoulpoor, S., Dokaneheifard, S., & Mohammadi, M. (2021). Hyaluronic acid-based drug nanocarriers as a novel drug delivery system for cancer chemotherapy: A systematic review. *Daru : Journal of Faculty of Pharmacy, Tehran University of Medical Sciences*, *29*(2), 439–447. https://doi.org/10.1007/s40199-021-00416-6
35. Santhamoorthy, M., Asaithambi, P., Ramkumar, V., Elangovan, N., Perumal, I., & Kim, S. C. (2025). A Review on the Recent Advancements of Polymer-Modified Mesoporous Silica Nanoparticles for Drug Delivery Under Stimuli-Trigger. *Polymers 2025, Vol. 17, Page 1640*, *17*(12), 1640. https://doi.org/10.3390/polym17121640
36. Satapathy, M. K., Yen, T. L., Jan, J. S., Tang, R. D., Wang, J. Y., Taliyan, R., & Yang, C. H. (2021). Solid Lipid Nanoparticles (SLNs): An Advanced Drug Delivery System Targeting Brain through BBB. *Pharmaceutics*, *13*(8). https://doi.org/10.3390/pharmaceutics13081183
37. Sharma, A., & Sharma, U. S. (1997). Liposomes in drug delivery: Progress and limitations. *International Journal of Pharmaceutics*, *154*(2), 123–140. https://doi.org/10.1016/S0378-5173(97)00135-X
38. Stanicki, D., Vangijzegem, T., Ternad, I., & Laurent, S. (2022). An update on the applications and characteristics of magnetic iron oxide nanoparticles for drug delivery. *Expert Opinion on Drug Delivery*, *19*(3), 321–335. https://doi.org/10.1080/17425247.2022.2047020
39. Stefanache, A., Lungu, I. I., Anton, N., Damir, D., Gutu, C., Olaru, I., Plesea Condratovici, A., Duceac, M., Constantin, M., Calin, G., Duceac, L. D., & Boev, M. (2025). Chitosan Nanoparticle-Based Drug Delivery Systems: Advances, Challenges, and Future Perspectives. *Polymers 2025, Vol. 17, Page 1453*, *17*(11), 1453. https://doi.org/10.3390/polym17111453
40. Suhail, M., Rosenholm, J. M., Minhas, M. U., Badshah, S. F., Naeem, A., Khan, K. U., & Fahad, M. (2019). Nanogels As drug-delivery Systems: a Comprehensive Overview. *Therapeutic Delivery*, *10*(11), 697–717. https://doi.org/10.4155/tde-2019-0010
41. Tajabadi, M. (2025). Application of Carbon Nanotubes in Breast Cancer Therapy. *Drug Research*, *75*(3–04), 89–93. https://doi.org/10.1055/a-0945-1469
42. Vangijzegem, T., Stanicki, D., & Laurent, S. (2019). Magnetic iron oxide nanoparticles for drug delivery: applications and characteristics. *Expert Opinion on Drug Delivery*, *16*(1), 69–78. https://doi.org/10.1080/17425247.2019.1554647
43. Vashist, A., Perez Alvarez, G., Andion Camargo, V., Raymond, A. D., Arias, A. Y., Kolishetti, N., Vashist, A., Manickam, P., Aggarwal, S., & Nair, M. (2024). Recent advances in nanogels for drug delivery and

biomedical applications. *Biomaterials Science*, *12*(23), 6006–6018. https://doi.org/10.1039/d4bm00224e

44. Verma, N., Arora, S., Singh, A. K., & Ahmed, J. (2025). Unlocking the potential of exosomes 'extracellular vesicles': drug delivery advancements and therapeutics in ocular diseases. *RSC Pharmaceutics*, *2*(6), 1201–1226. https://doi.org/10.1039/d5pm00097a
45. Wang, J., Li, B., Qiu, L., Qiao, X., & Yang, H. (2022). Dendrimer-based drug delivery systems: history, challenges, and latest developments. *Journal of Biological Engineering 2022 16:1*, *16*(1), 18-. https://doi.org/10.1186/s13036-022-00298-5
46. Wang, Q., Atluri, K., Tiwari, A. K., & Babu, R. J. (2023). Exploring the Application of Micellar Drug Delivery Systems in Cancer Nanomedicine. *Pharmaceuticals 2023, Vol. 16, Page 433*, *16*(3), 433. https://doi.org/10.3390/ph16030433
47. Yadav, D., Sandeep, K., Pandey, D., & Dutta, R. K. (2017). Liposomes for Drug Delivery. *Journal of Biotechnology & Biomaterials*, *7*(4), 1–8. https://doi.org/10.4172/2155-952x.1000276
48. Zhang, W., Zhang, Z., & Zhang, Y. (2011). The application of carbon nanotubes in target drug delivery systems for cancer therapies. *Nanoscale Research Letters*, *6*(1), 555. https://doi.org/10.1186/1556-276X-6-555