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ADVANCE DRUG DELIVERY SYSTEM AND MODERN TECHNIQUES

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ABSTRACT

This article provides an overview of the current state of advanced drug delivery systems and their potential to improve human health. We discuss the applications of these systems in various diseases, including cancer, diabetes, and neurological disorders, and also explore their potential to optimise drug delivery system design and performance. Advance drug delivery systems have revolutionized the way medications are administered, offering improved efficacy, reduced side effects, and enhanced patient compliance. This review highlights modern techniques in drug delivery, including nanotechnology, targeted delivery, and controlled release systems. We discuss the principles, applications, and benefits of these advanced systems, as well as their potential to transform the treatment of various diseases. Recent advancements in biomaterials, microfabrication, and computational modelling have enabled the development of sophisticated drug delivery systems that can respond to specific physiological cues, release drugs in a controlled manner, and target specific cells or tissues. Some type of drug delivery system that uses vesicles, which are small, fluid-filled sacs or bubbles, to encapsulate and deliver drugs. Vesicles can be made from various materials, including lipids, polymers, and proteins. This review highlights the latest advancements in advanced drug delivery systems, including stimuli-responsive systems, targeted delivery, and personalized medicine.

KEYPOINTS: ADDS, MT, MN, HPMC, PVP, PVA.

INTRODUCTION

Conventional drug delivery methods are marred by severe disadvantages like poor bioavailability, systemic toxicity, and ineffective tissue targeting, which make traditional drug delivery systems less potent in modern therapeutic regimens. To address such limitations, new drug delivery systems, centred on lipidic, proteic, and polymeric nanoparticles, have been developed to enhance drug stability, regulate release processes, and improve biodistribution. Material sciences have provided means to engineer biocompatible and multi-purpose drug carriers, some of which have been tested in clinical trials, with increased efficacy and reduced side effects.[1,2]

New technologies in drug delivery have shown immense potential in oncology, and various innovations have already begun to impact cancer therapies; many more await realisation. Rational design of anticancer delivery systems holds the potential to overcome limitations of conventional dosage forms.[3] Specifically, targeted drug delivery enhances therapeutic effectiveness by confining the drug to the target site, minimising exposure to nearby normal tissues. Effective distribution within the tumour mass is also essential; inefficient delivery provides residual tumour cells that sustain tumour regrowth and drug resistance.[4]

A Drug Delivery System (DDS) is a specialised device or formulation intended to guide the administration of therapeutic products into the body and their efficacy and safety profiles. This is done through strictly controlling the rate, timing, and site of drug release. Serves as a key interface between patient and drug, the DDS plays a pivotal role in maximising pharmacologic effects and reducing side effects.[5]

In the last several decades, tremendous progress in pharmaceutical sciences has resulted in the creation of more advanced delivery platforms. Some of these are, but not limited to, nanoparticles, microparticles, transdermal systems, inhalation products, subcutaneous implants, and antibody-drug conjugates. These innovations are designed to break through the barriers of traditional drug delivery approaches by enhancing bioavailability, targeting particular tissues, and allowing controlled or sustained release profiles.[6]

In spite of the intensified pace of DDS research and the spread of new technologies, translation to the clinic and marketplace of initial-stage discoveries is still an urgent challenge. Translating these systems from laboratory success to practical use is critical in order to unlock their

complete therapeutic value and maintain long-term interest and investment in the discipline.[7]

Classification of Advance drug delivery systems

Category	Sub-Category	Description
1. Particulate Drug Delivery	Polymeric Nanoparticle[8]	Spherical particles (10–1000 nm) made from biodegradable polymers (e.g., PLGA, chitosan). Offer high drug-loading capacity, controlled release, and tunable surface characteristics; used for targeting skin diseases, pulmonary infections, and ocular conditions.[8]
	Lipid-Based Nanoparticle[9]	SLNs are sub-200 nm particles with a solid lipid core; NLCs combine solid and liquid lipids for improved drug encapsulation and stability. Both enhance bioavailability, enable controlled release, and protect labile drugs from degradation.[10]
	Dendrimers	Highly branched, monodisperse macromolecules (1–10 nm) with multiple surface functionalities.[11] Facilitate precise drug conjugation or encapsulation; show promise for targeted delivery and reduced systemic toxicity[12]
	Polymeric Micelles	assembled amphiphilic block copolymers (10–100 nm) forming a hydrophobic core and hydrophilic shell. Useful for solubilising poorly water-soluble drugs, prolonged circulation, and passive tumour targeting via the Enhanced Permeability and Retention (EPR) effect[13]
2. Vesicular Delivery System	Liposomes	Phospholipid bilayer vesicles (50–200 nm) that encapsulate hydrophilic drugs in the aqueous core and hydrophobic drugs within the lipid bilayer. Provide biocompatibility, reduced toxicity, and the ability to modify surfaces with ligands for active targeting[14]
	Niosomes	Nonionic surfactant–based vesicles (50–300 nm) similar to liposomes, but with improved stability and lower production cost. Enhance drug permeation through biological barriers and are used for topical, oral, and parenteral routes[15]
	Ethosomes / Transfersomes	Ultra-deformable lipid vesicles (50–300 nm) containing high ethanol content (ethosomes) or edge activators (transfersomes) to enhance skin permeability. Particularly effective for transdermal delivery of small molecules and peptides[13]
	Invasomes	Phospholipid vesicles containing ethanol and terpene-based permeation enhancers (80–200 nm). Designed to overcome the stratum corneum barrier for improved transdermal delivery, showing enhanced skin penetration and controlled drug release
3. Inorganic Nanomaterials	Carbon nanotubes (CNTs) / Graphene Oxides (GO)	CNTs (1–100 nm diameter) and GO nanosheets offer high surface area, ease of functionalization, and intrinsic optical properties. Employed in tumour targeting (e.g., lung cancer) via the EPR effect, and as carriers for chemotherapeutics (e.g., doxorubicin conjugation) to enhance intracellular delivery and photothermal therapy[15]
4. Macroscopic Delivery System	Transdermal Patches (e.g., Micropatch, Invasome-based)	Patches comprising a drug reservoir, a rate-controlling membrane, an adhesive layer, and a backing. Provide steady systemic delivery through skin, bypass first-pass metabolism, improve patient compliance; invasome-based patches further enhance permeation via terpenes and ethanol[16]
	Implants (Biodegradable Polymer)	Subcutaneous or intramuscular rods/discs (e.g., PLGA implants) that provide sustained release over months. Used for hormonal therapies, local cancer treatment, and chronic pain management; reduces dosing frequency and maintains

		steady plasma levels[17]
	Oral Control Release System	Osmotic-pump-based tablet systems (OROS®) are designed for zero-order release; maintain predictable plasma concentrations over 24 hours. Improve therapeutic efficacy for drugs requiring tight control (e.g., cardiovascular agents) and reduce side effects [17]
	Implantable convection-enhanced Delivery	Direct infusion of therapeutic agents into the brain interstitium via pressure gradient; bypasses–brain barrier for glioblastoma treatment. Allows distribution over a larger volume; still under clinical investigation due to challenges with catheter placement and adverse events
5. Stimuli Responses System	pH-responsive carriers	Polymers or lipids engineered to undergo conformational change or degradation at acidic pH (e.g., tumour microenvironment pH 5.0–6.5). Enable targeted release in cancerous tissues or endosomal compartments; examples include pH-sensitive hydrogels, micelles, and nanoparticles[18]
	Redox-responsive carrier	Systems containing disulfide linkages that are cleaved by high intracellular glutathione (GSH) levels (especially in tumour cells). Upon entering the reductive cytosol, carriers disassemble and release payload; widely applied in polymeric micelles and nanoparticle platforms for anticancer agents[18]
	Temperature-Sensitive (thermo-responsive system	Carriers (hydrogels, NPs, liposomes) that undergo a phase change or increased permeability at mild hyperthermia (≥40 °C).[19]
	Enzyme-responsive carriers	Smart carriers with linkers or coatings cleaved by disease-associated enzymes (e.g., MMPs in tumours, phospholipases in inflamed tissue).[20]
6. Physical / Device-Based Delivery System	Microneedle	**Solid MN + Patch:** Create microchannels, then apply drug patch (e.g., DNA vaccines). **Coated MN:** Microparticle or liquid coating on MN surface (e.g., influenza antigen). **Hollow MN:** Microfluidic injection into dermis (e.g., insulin delivery). **Dissolving MN:** Fabricated from dissolvable polymers (e.g., hyaluronic acid, PVA) carrying vaccines, peptides, or biopharmaceuticals; upon insertion, needles dissolve, releasing cargo (e.g., COVID-19 vaccine candidates). **Stimuli-Responsive MN:** pH- or enzyme-responsive materials integrate with MN (e.g., MMP-sensitive hydrogel MN for tumour therapy) for on-demand release[21]
	Nasal spray / Intranasal device	**Standard Metered**-Dose Sprays: Deliver solution or suspension into the nasal cavity (e.g., sumatriptan nasal spray for migraines). **Bi-Directional Devices:** Breath-actuated to target olfactory/cerebrospinal ducts, minimising lung deposition (e.g., for CNS therapeutics). **Spray-Freeze-Dried (SFD) Powders:** Rapid dispersal in the nasal cavity (e.g., intranasal insulin powders). **Smart Hydrogel Sprays:** Thermosensitive or mucoadhesive formulations that gel in the nasal cavity to prolong residence (e.g., allergic rhinitis treatments).

		Nanoparticle-Enabled Nasal Devices: Lock nucleic acid vaccines in NPs for intranasal immunisation against respiratory viruses.[22]
	Programmable / Implantable Pumps (Micropumps & Osmostic Pumps)	**Programmable Micro-Infusion Pumps (e.g., iPRECIO®):** Refillable, programmable, implantable for precise PK/PD studies (e.g., rat models of infusion). **MEMS-Based Micropumps:** Piezoelectric, electroosmotic, or peristaltic micropumps integrate with microfluidics for on-demand dosing (e.g., inner ear gentamicin delivery). **Implantable Smart Pumps:** Wireless control to adjust infusion rate (e.g., insulin delivery in diabetic models).[23]

Particulate Drug Delivery - It is a type of drug delivery system that comprises small devices or nanoscale carriers to deliver the desired compound into the system. These generally range from 1-1000µm micro or 1-1000nm nanoscale, respectively. These carriers are Polymeric Nanoparticle, Dendrimers, Polymeric Micelles, Metal Organic Framework and Nanocrystals; they can be designed in a different material depending on the drug characteristics and delivery site.[24] It provides several benefits over traditional drug delivery systems, such as Improved Solubility, Control and sustained release, Targeted Delivery and Bypassing of Barriers.[25]

Application of Particulate Drug Delivery System

Cancer Therapy – Doxorubicin and Paclitaxel (Taxane class of drug highly active agent used in the treatment of Breast Cancer), these are loaded with micelles to improve solubility and reduce hypersensitivity.[26]

Central Nervous System disorders – Controlled release and minimum dose frequency can maintain therapeutic levels in brain tissues. Rivastigmine (a Cholinesterase inhibitor class of drug) loaded with nanoparticles results in improved brain uptake in Alzheimer's Patients.[27]

- Ocular Drug Delivery – Intraocular Injections deliver sustained release of drug in anterior and posterior eye segments in diseases such as glaucoma, macular degeneration and uveitis. Triamcinolone loaded with PLGA [poly (lactic-co-glycolic acid)] showed sustained release of retinal drug, which results in reduced inflammation.[28]
- Pulmonary Drug Delivery – For localised treatment with minimal systemic exposure of drug macroparticles and nanoparticles are inhaled in dry form, which are then deposited in the deep lungs. siRNA (small interfering RNA) can be efficiently delivered by inhalable PLGA microparticles for lung cancer cells, which further leads to gene silencing and tumour suppression.[29]
- Vaccine Delivery – Biodegradable Polymeric Nanoparticle, such as PLGA and Chitosan, protect the antigen and stimulates humoral and cellular immunity, e.g. the mRNA vaccine developed by Pfizer/BioNTech and Moderna used this technique, lipid Nanoparticle as a delivery system for the mRNA into the host cell, the mRNA strand was protected by lipid Nanoparticle encapsulation.[30]

Vesicular Delivery System – The delivery systems which utilizes vesicles (It is a small mainly formed by membrane and filled with liquids) to deliver drug into the systems, in which drug is encapsulated within a vesicle that is spherical structure, microscopic can be designed to encapsulate various nature of drugs such as hydrophilic (water soluble), Lipophilic (fat soluble) and Amphipathic (it is both water loving and water repelling in nature). These systems are specifically used to assess drug efficacy, bioavailability and targeted delivery.[31][32]

Types of Vesicular Drug Delivery Systems

A. Lipid-Based Vesicular Systems

Vesicular System	Composition/Structure	Mechanism of Action	Application
Liposomes[33]	Phospholipid bilayer-forming vesicle with aqueous core	Hydrophilic drug in the core / lipophilic in the bilayer	Cancer therapy (Doxil) Antifungal (AmBisome)
Niosomes[34]	Non-Ionic Surfactants + Cholesterol / Surfactant-based vesicle	Hydrophilic drug in core / Lipophilic drug in Bilyer	Transdermal/Topical gels (ketoconazole) Gene Delivery System
Ethosomes[35]	Phospholipid + Ethanol (20-40%)	Ethanol fluidises skin lipids (stratum corneum) and increases vesicle flexibility to penetrate deeper layers; enhances transdermal flux.	Antiviral (Acyclovir) Hormone Peptide Transdermal delivery of analgesics (difunisal)
Tranferosomes[36][37]	Phospholipids + edge activators	Ultra-deformable vesicles that	Transdermal insulin, anti-

	(sodium deoxycholate, Tween 80)	squeeze through skin intercellular pathways (<50 nm) without rupturing; enhanced permeation and deeper tissue delivery	inflammatories (diclofenac)
Ufasomes[38]	Unsaturated fatty acids (oleic acid) at physiological pH form closed bilayer vesicles	Form vesicles at physiological pH; pH-sensitive release and biocompatible lipid interaction enhance drug entrapment and skin uptake	Topical NSAID delivery (ibuprofen)
Bilosomes[39]	Lipid vesicles with incorporated bile salts (e.g., sodium deoxycholate), sometimes with surfactants	Bile salts stabilise vesicles in the GI tract and promote uptake via Peyer's patches; enhance oral delivery and mucosal immunogenic response	Oral vaccines (hepatitis B antigen) - Oral peptide/protein delivery (insulin)

B. Non-Lipid-Based Vesicular Drug Delivery System

Vesicular System	Composition/Structure	Mechanism of Action	Application
Polymersomes[40]	Self-assembled vesicles from amphiphilic block copolymers [PEG-b-PDPA (poly (ethylene glycol)-block-poly(2-(diisopropylamino)ethyl methacrylate) and PEG-b-PLA (Poly (ethylene glycol)-block-poly(D,L-lactic acid)]	Encapsulate hydrophilic cargo in the aqueous lumen and hydrophobic drugs within the membrane, stimuli-responsive (pH, redox, temp) disassembly triggers payload release, then PEG corona limits clearance	Cancer therapy (co-delivery of siRNA + chemotherapeutics)
PICsomes[41]	Polyion complex vesicles assembled from PEG-b-PAsp and P(Asp-AP)	Encapsulate enzymes/proteins in an aqueous core, release triggered by intracellular conditions or enzyme activity	Therapeutic enzyme delivery (e.g., L-asparaginase with prolonged half-life)
Theranostic Polymersomes[42]	Polymersomes embedded with inorganic nanoparticles (magnetic iron oxide, gold nanorods)	Multimodal delivery: MR imaging contrast + magnetically or photothermally triggered drug release (doxorubicin)	Combined cancer imaging and therapy (guided chemotherapeutics via magnetic or photothermal triggers)
Aquasomes[43]	Tri-layered nanoparticles: ceramic core (e.g., silica), oligomer coat, and drug adsorbed as a surface layer	Stabilise and preserve bioactive molecules on the surface; protect proteins from denaturation; release via desorption or biodegradation.	Delivery of antigenic proteins, insulin, and haemoglobin is useful for oral and injectable vaccines or sensitive biomolecules.

C. Amphipathic Vesicle System

Vesicular System	Composition/Structure	Mechanism of Action	Application
Peptide Amphiphile Vesicles[44]	Peptide-based amphiphiles (TAT-peptide with disulfide bridges) self-assembled into vesicles	GSH-responsive disulfide bonds trigger cargo release in reductive intracellular environments.	Anticancer drug delivery—sustained release in tumour cells
Protein-Polymer Amphipathic Vesicles[45]	Amphipathic peptides (ApoA1 mimetic L4F) fused to elastin-like polypeptides form ~50 nm unilamellar vesicles	Amphiphilic assembly into vesicles, inherent bioactivity of peptide, stable circulation, uptake by target cells	Anti-inflammatory and anti-fibrotic activity in liver stellate cells; potential for therapeutic protein delivery
Polymersome[46]	Amphiphilic block copolymers (e.g., PEG-b-PDPA, PEG-b-PLA) self-assemble into bilayer vesicles with a hydrophilic shell and a hydrophobic membrane	Encapsulation of hydrophilic and hydrophobic drugs - stimuli (pH/redox/temperature)-responsive disassembly - surface functionalization for targeting	Cancer therapy (co-delivery of chemotherapeutics and siRNA), intracellular protein/peptide delivery
Polymeric Chitosan Amphiphiles[47]	Glycol-chitosan chemically modified with fatty-acid chains (~11–16	Amphiphilic self-assembly, mucoadhesive and membrane,	Oral/intranasal delivery of gut-labile molecules

	mol% %) forms unilamellar vesicles alongside cholesterol	permeating properties - entrap hydrophilic drugs via gradient loading.	(bleomycin)
Hybrid Amphiphilic Vesicles[48]	Hybrid vesicles combining peptides, polymers, and macrocycles (leucine‑zipper peptides + polymersomes)	Heat- or stimuli-triggered vesicle disruption; amphiphilic peptide domains confer thermosensitivity and cargo release upon heating	Thermo-responsive cancer drug delivery (doxorubicin release under hyperthermia) with targeted uptake via peptide ligands)

Inorganic Nanoparticle Drug Delivery – An inorganic nanoparticle is the combination of one or two different types of inorganic material with the same or different properties, together with a physical or chemical method to exert different properties. Inorganic Nanomaterials lie in the scale of 1-100nm and comprise inorganic materials like Metal, Metal Oxides, Gold nanoparticles (AuNPs), Mesoporous silica, carbon-based nanoparticles (CNTs) and Magnetic nanoparticles. All these give diverse properties, robust functionality and theranostic capability.[49][50]

Nanoparticle	Properties	Mechanism of Action	Application
AuNPs	Highly stable	Coated AuNPs are conjugated with drug molecules via thiol linkage or adsorbed onto them.	Cancer therapy, Imaging radiolabel Disease markers delivery[51]
Mesoporous Silica	High surface area, Uniform tunable pore size	Drugs are loaded into the pores, then it was capped with stimuli-sensitive materials.	Cancer drug delivery (doxorubicin, paclitaxel)
CNTs	High aspect ratio, planar surface area	Drugs are loaded via noncovalent interactions between the pi bonds (π–π) [52]	Delivery of siRNA, Tissue Engineering
Magnetic (Iron Oxides)	Superparamagnetic iron oxide cores	Loaded drugs are targeted to the site by an external magnetic field. Release can also be triggered by local stimuli or a magnetic field.	Magnetically guided site-specific therapies [53]

Macroscopic Delivery System – It is an approach to a drug delivery system in which a drug can be delivered using larger-scale systems or structures to deliver it to the targeted site. These systems and structures can vary in various forms, such as implants, patches, injections, or it can be as simple as oral tablets. This delivery system aims to deliver the drug to the specific target site, improve bioavailability and show controlled release.

Table – Comparative analysis of Scales of Drug Delivery.

Properties	Macroscopic Systems	Microscopic Systems	Nanoscopic Systems
Size Range	> 100 µm to cm scale	1 µm - 1000 µm	1 nm - 1000 nm
Surface Area: Volume	Low	Intermediate	High
Administrative Route	Oral (tablets), Implantation (implants, stents), Topical (patches).	Parenteral (injectable microparticles), Oral (microcapsules), Inhalation.	Parenteral (IV injection), Oral, Topical.
Advantages	Prolonged, predictable, and often zero-order release over long durations.	Good for depot injections, can improve solubility and protect drugs from degradation.	Enhanced tissue penetration, cellular uptake, targeted delivery, and delivery of biologics.[54]

Table – Macroscopic drug delivery systems

Systems	Structure	Mechanism of Action	Application
Transdermal Patches [55][56]	Multiple Layer Polymer – Drug Reservoir or Matrix, Rate controlling and Adhesive	Control Diffusion via membranes into the skin	Hormone replacement therapy, Nicotine Replacement therapy and Cardiovascular drugs
Biodegradable implants [56][57]	Rods and discs are made up of biodegradable polymers then which are then implanted subcutaneously and intramuscularly.	Drugs released via erosion and diffusion methods by polymers	Contraceptives, Chronic pain management therapies, orthopaedic surgeries and cancer therapies.
Osmotic Pumps implantable [58]	Semipermeable	Drug Release initiates	Administration of

	membranes and osmotic engines (Alzet, SynchroMed)	via osmotic pressure (zero-order drug release)	Chemotherapy drugs and Chronic pain therapy
Programmable Infusion Pump / MEMS (Micro-Electro-Mechanical Systems)[59][60]	Electronic or Mechanical implants, Pumps and Reservoirs (peristatic, piezoelectric and piezoactuated)	Electronically Programmed Systems and Dose-Controlled Infusions	Insulin delivery in type-1 diabetes, chemotherapy, and ocular infusion
Convection-Enhanced Delivery (CED)[61][62]	Catheter systems that deliver a drug into the brain tissue by pressure	Pressure-driven infusion that distributes the drug into tissues	Glioblastoma therapy

Stimuli Responsive Drug Delivery System (SRDDS) – SRDDS is a type of advanced formulation which are engineered to release the drugs or compounds in a precise spatiotemporal manner in response to any specific physiological or biological triggers, which can be internal or external. This smart approach to drug delivery enables many options in the field of controlled drug release, site-specific and on-demand release of therapeutics. By minimising off-target exposures and improving synchronised delivery, this system can have improved efficacy and safety.[63][64][65]

Internal Stimuli Response System – These systems respond to physiological and biochemical factors that are inherent to the body or which is uniquely characteristic of a pathological environment. These are mainly included changes in the pH levels, fluctuation in redox potential, specific or general enzyme activities and changes in the concentration of any biomolecules or biofluids.[64][66][67]

External Stimuli Response System – They are activated by external triggers or applications, mostly non-invasive energy sources, triggers such as temperature, light, application of magnetism and exposure to sounds.[63][68]

Table – Comparison between Internal and External Stimuli.

Properties	Internal Stimuli	External Stimuli
Control	Drug release is determined by the body's internal response or triggers	Drug release controlled by externally applied triggers and applications
Mechanism of response	Responds to biological triggers such as pH, enzymes, and concentration	Responds to physical energies such as heat, light, magnetic, sound, and temperature
Spatiotemporal Precision	Spatially precise	High precision
Drug distribution	Easily distributed requires no external hardware or activation.	It requires external factors for activation; thus, distribution depends.
Applications	Used in chronic diseases where continuous and adaptive management is required.	Acute and localised treatment where precise time and duration are necessary.

Table – Types of Stimuli-responsive systems.

Type	System	Mechanism of action	Applications
pH-Responsive	pH-sensitive micelles, Super-porous PEG-PLGA	Material swells or degrades under specific pH conditions, such as – 5-6.8 in tumour, 6 in endosomes.	Targeted chemotherapy, gastroretentive formulations[69]
Redox Responsive	Disulfide-linked polymers (PEG-PDPA	The difference in redox potential between normal and target cells. Intracellular Glutathiones (GSH) cleave disulfide bonds that cause vesicle rupture, resulting in rapid drug release.	Enhanced tumour selectivity, High intracellular doxorubicin delivery[70][71]
Temperature Responsive	PNIPAM [Poly(N-isopropylacrylamide)] based hydrogel, Magnetic Hydrogel	Polymers with a lower critical solution temperature (LCST) between 37-42°C can change from soluble to gel or even deformed when heated, by inducing magnet nanoparticle	In-situ forming gel[72]
Enzyme Responsive	MMP-sensitive polymer nanocarrier	It is triggered by enzyme-catalysed reactions; it binds to a	Controlled site-specific release in tumours or

		recognisable element, which initiates a certain chemical reaction in the polymer or nanocarriers, leading to the release of drugs.	wounds[73]
Dual / Multi Stimuli System	Hybrid polymer nanocomposites that are responsive to pH and redox	These systems are designed to release certain drugs in sequence or series, with one trigger releasing one drug while other stimuli trigger the second drug	Improve tumour uptake and cytotoxicity through coordinated release[74][75]

Physical / Device-based drug delivery system

In this system, physical forces or devices are used to deliver the medication or other therapeutic substances into the body. These systems are relying on the physical mechanism, an external energy source and integrated mechanical devices to achieve control, targeted, site-specific or on-demand release of the drug into the body. By overcoming the limits of traditional medications like tablets, capsules, ointments, and other liquid dosage forms, these systems primarily focus on the active manipulation of the pharmacokinetic and pharmacodynamic profile of the drug, maximising the therapeutic activity and reducing the adverse effects of drugs.[76]

A. Microneedle (MN) Array – These are used for transdermal drug delivery system which consist of 100-1000 µm in length that are pierce the outmost layer of the skin (stratum corneum) but are short enough to stimulate nerve endings that are usually located in deeper section of the skin, through this drug can bypass skin physiological barrier.[77][78]

Type of MN	Structure / Material	Delivery Mechanism	Application
Solid MNs	Rigid and sharp, Needles are made up of silicon metals	It first punctures the skin, and then drugs are applied externally via formulations.	Transdermal vaccination, Collagen induction therapy[78][79]
Coated MNs	Core – Solid (metal or polymer) Coating – a thin layer of drug or formulation	When the MNs penetrate the skin surface, the coated drug gets dissolved into the tissues.	Vaccine Delivery (Influenza), Insulin, Multi-drug patches[79][80]
Hollow MNs	Internal lumen (5-70µm) Made up of silicon, polymer and metal	Liquid content inside the hollow space was dispersed into the skin once applied.	High dose delivery, Insulin, therapeutic proteins[81][82]
Dissolving MNs	Water-soluble, bio-degradable polymers (PVA, PVP and Hyaluronic)	MNs were dissolved into the skin when injected, releasing the drugs	Wound Healing, Cosmetic, Cancer treatment[79][81]
Hydrogel Forming MNs	Crosslinked Polymers (chitosan, PVA) swell when hydrated by interstitial fluids.	When contacting interstitial fluids, the hydrogel swells and opens a pathway for drugs or formulations that are released into circulation.	Sustained delivery of macromolecules, Biosensors, Wound Healing[83]

B. Implantable / Programmable pumps – Implantable devices are advanced medical instruments that are surgically implanted in the body. They are used to deliver a specific amount of drug and formulations, monitor various vital stats, monitor health and condition of the body or enhance specific body functions through custom physicochemical changes.[84][85][86]

Programmable implantable infusion pumps (PIIPs) – These are used to deliver precise and controlled doses of formulation and drugs into the body. These are mainly used to deliver medication for diabetes patients and conditions such as pain, hormone and other therapeutic uses. Examples are SynchroMed and PROMETRA

Active Implantable Medical Devices (AIMDs) – These are the devices implanted into the body to monitor various physiological changes and vitals. These are externally powered for energy or require in-time updates.

- Pacemaker for maintaining heart rhythm[87]
- Neurostimulators – they trigger brain cells by stimulating a specific electrical signal to the targeted cell for the treatment of brain disorders[87]
- Implantable Cardioverter defibrillator – Monitors heart rhythm and can deliver an electrical impulse in specific conditions[87]

Pumps	Delivery Method	Application	Products
Electromechanical Pump	Continuous bolus or programmable pulsatile infusion	Chemotherapy. Pain Management therapy,	SynchroMed (Medtronic)[88] Infusor (Baxter)

		Hormone therapy	Crono P (Cane)
Osmotic Pumps	Controlled release with adjustable interval time	Cancer, Diabetes, Cardiovascular condition	DUROS (Alza/Intarcia)[88] Viadur
Micro-Electro-Mechanical Pumps	Scheduled release of precise doses	Osteoporosis, Vaccination, Neurological diseases	MicroCHIPS implants[89][90]
Infusion Pumps	Subcutaneous or Intrathecal infusion	Insulin therapy, Antibiotics, Parkinson's (apomorphine)	Omnipod DASH (Insulet) t: slim X2 pump[91]
Smart Pumps	Feedback-regulated controlled-release infusion	Diabetes management, Personalized medicine	Medtronic MiniMed 780G, iLet Bionic Pancreas[92]

C. Intranasal Device-Based Delivery System – These are the system that deliver medication or formulation directly into the nasal cavity, these are designed to optimize drug deposition, absorption, and bioavailability all across the nasal mucosa.[93]

1. Standard Metered Spray – It is a device that are designed to deliver a precise and consistent amount of formulation and liquid medication with every actuation, this liquid formulation is forced through a meter valve, which creates droplets comprise a size of 25-200µL. Examples are Fluticasone, mometasone nasal spray for rhinitis and congestion.[93]
2. Bidirectional (Breath powered Device) – It works by exhaled breath to deliver the aerosols into the deeper section, posterior regions such as the olfactory cleft. When the patient exhaled into the mouthpiece, their soft palates close at the same time aerosols are delivered across the nasal passage into the bidirectional flow, preventing medication from going into the lungs and throat. Examples are OptiNose Xhance, Onzetra Xsail.[94]
3. Spray Freeze Dried Powdered Device – These devices are used to deliver lyophilized or freeze-dried powder into the nasal cavities, the fine droplets of nasal spray is freeze dried then sublimating these droplets into solvents to produce powders, which is porous spherical particles that has larger surface area, these particles show enhanced stability (Physical and Chemical) compared to conventional aerosols, reducing the half life and deliver enhance effects. These are activated by the patient's breath or in contact with the mucosa in the posterior regions. Examples are the Delivery of monoclonal antibodies (anti-SARS-CoV-2 mAb)[95]
4. Smart Hydrogel Spray – Smart Hydrogels are biomaterials (polymers) that are activated in certain stimuli or biochemical changes in the environment, like they can change their properties according to changes in pH, temperature, and concentration. It can swell or contract when the physiological changes occur, with the ability to adhere to the nasal mucosa, which will help to increase the time of contact from the nasal line with the drug, giving enhanced and prolonged effects.[96]

CONCLUSION

In conclusion, advanced drug delivery systems and modern techniques have transformed the pharmaceutical landscape, offering improved therapeutic outcomes, enhanced patient compliance, and reduced side effects. The integration of cutting-edge technologies, including nanotechnology, biomaterials, and 3D printing, has enabled the development of targeted, controlled, and personalized drug delivery systems. As research continues to evolve, these advancements hold great promise for improving human health and addressing unmet medical needs. Advanced drug delivery systems and modern techniques have revolutionized the field of pharmaceuticals, enabling targeted, controlled, and efficient delivery of therapeutic agents. The integration of nanotechnology, biomaterials, and other cutting-edge technologies has improved the efficacy and safety of drug delivery systems. As research continues to advance, we can expect the development of even more sophisticated and personalised drug delivery systems. These systems will likely play a critical role in improving patient outcomes and transforming the treatment of various diseases.

REFERENCES

1. El-Tanani, Mohamed, Shakta Mani Satyam, Syed Arman Rabbani, Yahia El-Tanani, Alaa A. A. Aljabali, Ibrahim Al Faouri, and Abdul Rehman. "Revolutionising Drug Delivery: The Impact of Advanced Materials Science and Technology on Precision Medicine" Pharmaceutics, 2025; 17(3): 375. https://doi.org/10.3390/pharmaceutics17030375
2. Martinho, Nuno, Christiane Damgé, and Catarina Pinto Reis. "Recent advances in drug delivery systems." Journal of biomaterials and nanobiotechnology, 2011; 2(05): 510.
3. Shenoy, Dinesh B., and Mansoor M. Amiji. "Poly (ethylene oxide)-modified poly (ε-caprolactone) nanoparticles for targeted delivery of tamoxifen in breast cancer." International Journal of Pharmaceutics, 2005; 293(1-2): 261-270.
4. Van Vlerken, Lilian E., Zhenfeng Duan, Steven R. Little, Michael V. Seiden, and Mansoor M. Amiji. "Biodistribution and pharmacokinetic analysis of Paclitaxel and ceramide administered in multifunctional polymer-blend nanoparticles in drug-resistant breast cancer model." Molecular Pharmaceutics, 2008; 5(4): 516-526.
5. Jain, Kewal K. "Drug delivery systems-an overview." Drug delivery systems, 2008; 1-50.
6. Anselmo, Aaron C., and Samir Mitragotri. "An overview of clinical and commercial impact of drug delivery systems." Journal of Controlled Release, 2014; 190: 15-28.

7. Sosnik, Alejandro, Diego A. Chiappetta, and Ángel M. Carcaboso. "Drug delivery systems in HIV pharmacotherapy: what has been done and the challenges standing ahead." Journal of Controlled Release, 2009; 138(1): 2-15.
8. Lopez-Vidal, Lucía et al. "Advanced drug delivery systems for the management of local conditions." Therapeutic delivery, 2025; 16(3): 285-303. doi:10.1080/20415990.2024.2437978
9. Jamroży, M., Kudłacik-Kramarczyk, S., Drabczyk, A., & Krzan, M. Advanced Drug Carriers: A Review of Selected Protein, Polysaccharide, and Lipid Drug Delivery Platforms. International journal of molecular sciences, 2024; 25(2): 786. https://doi.org/10.3390/ijms25020786
10. Jamroży, M., Kudłacik-Kramarczyk, S., Drabczyk, A., & Krzan, M. Advanced Drug Carriers: A Review of Selected Protein, Polysaccharide, and Lipid Drug Delivery Platforms. International journal of molecular sciences, 2024; 25(2): 786. https://doi.org/10.3390/ijms25020786
11. Karadurmus, Leyla, and Ali Serol Erturk. "Recent emerging trends in dendrimer research: Electrochemical sensors and their multifaceted applications in biomedical fields or healthcare." Biosensors and Bioelectronics, 2025; 117172.
12. Anand Singh Chouhan, Anubha Gupta, Garima Maurya, Shubhyanka Singh, A Review On Novel Drug Delivery Systems, Int. J. of Pharm. Sci., 2024; 2(7): 2121-2135. https://doi.org/ 10.5281/zenodo.13126249
13. Shubham Mane, Vidya Kale, A Review on Novel Drug Delivery System, Int. J. of Pharm. Sci., 2024; 2(6): 1099-1111. https://doi.org/10.5281/zenodo.12491082
14. Anand Singh Chouhan, Anubha Gupta, Garima Maurya, Shubhyanka Singh, A Review On Novel Drug Delivery Systems, Int. J. of Pharm. Sci., 2024; 2(7): 2121-2135. https://doi.org/ 10.5281/zenodo.13126249
15. Fu, Jiang MMa,b; Yu, Li MMc; Wang, Zixu MMa,b; Chen, Haoyu MMa; Zhang, Song MMa; Zhou, Haining MDa,b,d,*. Advances in controlled release drug delivery systems based on nanomaterials in lung cancer therapy: A review. Medicine, February 07, 2025; 104(6): e41415. | DOI: 10.1097/MD.0000000000041415
16. Anselmo, A. C., & Mitragotri, S. An overview of the clinical and commercial impact of drug delivery systems. Journal of controlled release: official journal of the Controlled Release Society, 2014; 190: 15–28. https://doi.org/10.1016/j.jconrel.2014.03.053
17. Anselmo, A. C., & Mitragotri, S. An overview of the clinical and commercial impact of drug delivery systems. Journal of controlled release: official journal of the Controlled Release Society, 2014; 190: 15–28. https://doi.org/10.1016/j.jconrel.2014.03.053
18. Hatakeyama, H. Recent advances in endogenous and exogenous stimuli-responsive nanocarriers for drug delivery and therapeutics. Chemical and Pharmaceutical Bulletin, 2017; 65(7): 612-617.
19. Khan B, Arbab A, Khan S, et al. Recent progress in thermosensitive hydrogels and their applications in the drug delivery area. MedComm – Biomater Appl., 2023; 2: e55. doi:10.1002/mba2.55
20. Liu, D., Yang, F., Xiong, F., & Gu, N. The Smart Drug Delivery System and Its Clinical Potential. Theranostics, 2016; 6(9): 1306–1323. https://doi.org/10.7150/thno.14858
21. Nguyen HX, Banga AK. Advanced transdermal drug delivery system: A comprehensive review of microneedle technologies, novel designs, diverse applications, and critical challenges. Int J Pharm., 2025 Feb 10; 670: 125118. doi: 10.1016/j.ijpharm.2024.125118. Epub 2024 Dec 20. PMID: 39710310.
22. Luo D, Ni X, Yang H, Feng L, Chen Z, Bai L. A comprehensive review of advanced nasal delivery, especially insulin and calcitonin. Eur J Pharm Sci., 2024.
23. Bhardwaj, Harish, and Rajendra Kumar Jangde. "Current updated review on preparation of polymeric nanoparticles for drug delivery and biomedical applications." Next Nanotechnology, 2023; 2: 100013.
24. Aminu, Nafiu, Idris Bello, Nura Muhammad Umar, Nuhu Tanko, Abdulmalik Aminu, and Momoh Mumuni Audu. "The influence of nanoparticulate drug delivery systems in drug therapy." Journal of drug delivery science and technology, 2020; 60: 101961.
25. Maeda, Hiroshi, Jun Wu, Tomohiro Sawa, Yasuhiro Matsumura, and Katsuyoshi Hori. "Tumour vascular permeability and the EPR effect in macromolecular therapeutics: a review." Journal of Controlled Release, 2000; 65(1-2): 271-284.
26. Saraiva, Cláudia, Catarina Praça, Raquel Ferreira, Tiago Santos, Lino Ferreira, and Liliana Bernardino. "Nanoparticle-mediated brain drug delivery: Overcoming blood–brain barrier to treat neurodegenerative diseases." Journal of Controlled Release, 2016; 235: 34-47.
27. Kumar Teli, Mahesh, Srinivas Mutalik, and G. K. Rajanikant. "Nanotechnology and nanomedicine: going small means aiming big." Current Pharmaceutical Design, 2010; 16(16): 1882-1892.
28. Mansour, H. M., Sood, A. K., & Dalhaimer, P. Nanoparticle-based therapeutics for pulmonary diseases. Nanomedicine, 2009; 4(4): 301-315. doi:10.2217/17435889.4.4.301
29. Pardi, Norbert, Michael J. Hogan, Frederick W. Porter, and Drew Weissman. "mRNA vaccines—a new era in vaccinology." Nature Reviews Drug Discovery, 2018; 17(4): 261-279.
30. Batur, E., Özdemir, S., Durgun, M. E., & Özsoy, Y. Vesicular Drug Delivery Systems: Promising Approaches in Ocular Drug Delivery.

Pharmaceuticals (Basel, Switzerland), 2024; 17(4): 511. https://doi.org/10.3390/ph17040511
31. Kapoor, Bhupinder, Reena Gupta, Monica Gulati, Sachin Kumar Singh, Rubiya Khursheed, and Mukta Gupta. "The Why, Where, Who, How, and What of the vesicular delivery systems." Advances in colloid and interface science, 2019; 271: 101985.
32. Sai, Ganesh & Gadela, Radha. (2021). NOVEL VESICULAR DRUG DELIVERY SYSTEMS: A REVIEW, 2021; 11. 10.5281/zenodo.4772544.
33. Chen S, Hanning S, Falconer J, Locke M, Wen J. Recent advances in non-ionic surfactant vesicles (niosomes): Fabrication, characterisation, pharmaceutical and cosmetic applications. Eur J Pharm Biopharm., 2019 Nov; 144: 18-39. doi: 10.1016/j.ejpb.2019.08.015. Epub 2019 Aug 22. PMID: 31446046.
34. Priya, Sakshi, Vaibhavi Meghraj Desai, and Gautam Singhvi. "Surface modification of lipid-based nanocarriers: a potential approach to enhance targeted drug delivery." ACS omega, 2022; 8(1): 74-86.
35. Batur, Eslim, Samet Özdemir, Meltem Ezgi Durgun, and Yıldız Özsoy. "Vesicular drug delivery systems: promising approaches in ocular drug delivery." Pharmaceuticals, 2024; 17(4): 511.
36. Abd El-Alim SH, Kassem AA, Basha M, Salama A. Comparative study of liposomes, ethosomes and transfersomes as carriers for enhancing the transdermal delivery of diflunisal: In vitro and in vivo evaluation. Int J Pharm., 2019 May 30; 563: 293-303. doi: 10.1016/j.ijpharm.2019.04.001. Epub 2019 Apr 2. PMID: 30951860.
37. Arundhasree, Rajalakshmi, R. Aiswarya, A. R. Kumar, S. Kumar, and S. Nair. "Ufasomes: Unsaturated fatty acid-based vesicular drug delivery system." Int. J. Appl. Pharm, 2021; 13(2): 76-83.
38. Kaurav H, Tripathi M, Kaur SD, Bansal A, Kapoor DN, Sheth S. Emerging Trends in Bilosomes as Therapeutic Drug Delivery Systems. Pharmaceutics., 2024 May 23; 16(6): 697. doi: 10.3390/pharmaceutics16060697. PMID: 38931820; PMCID: PMC11206586.
39. Lee JS, Feijen J. Polymersomes for drug delivery: design, formation and characterisation. J Control Release, 2012 Jul 20; 161(2): 473-83. Doi: 10.1016/j.jconrel.2011.10.005. Epub 2011 Oct 14. PMID: 22020381.
40. Qiu, Min, and Chao Deng. "Engineering polymersomes for intracellular biopharmaceutics delivery."
41. Sanson, Charles, Odile Diou, Julie Thevenot, Emmanuel Ibarboure, Alain Soum, Annie Brûlet, Sylvain Miraux et al. "Doxorubicin-loaded magnetic polymersomes: theranostic nanocarriers for MR imaging and magneto-chemotherapy." ACS nano, 2011; 5(2): 1122-1140.
42. Jain, Sanjay S., Pramod S. Jagtap, Neha M. Dand, Kisan R. Jadhav, and Vilasrao J. Kadam. "Aquasomes: A novel drug carrier." Journal of Applied Pharmaceutical Science Issue, 2012; 184-192.
43. Kim, Hayeon, Inhye Kim, Jun Ho Hwang, Jaehyun Park, Hyungju Ahn, Eun Hee Han, and Eunji Lee. "Glutathione-adaptive peptide amphiphile vesicles rationally designed using positionable disulfide-bridges for effective drug transport." Polymer Chemistry, 2020; 11(28): 4547-4556.
44. Pastuszka MK, Wang X, Lock LL, Janib SM, Cui H, DeLeve LD, MacKay JA. An amphipathic alpha-helical peptide from apolipoprotein A1 stabilises protein polymer vesicles. J Control Release, 2014 Oct 10; 191: 15-23. Doi: 10.1016/j.jconrel.2014.07.003. Epub 2014 Jul 10. PMID: 25016969; PMCID: PMC4327866.
45. Li, Dan, Xi Zhang, Xiao Chen, and Wei Li. "Research progress and prospects for polymeric nanovesicles in anticancer drug delivery." Frontiers in Bioengineering and Biotechnology, 2022; (10): 850366.
46. Uchegbu, Ijeoma F., Andreas G. Schätzlein, Laurence Tetley, Alexander I. Gray, Julieann Sludden, Soryia Siddique, and Erasto Mosha. "Polymeric chitosan-based vesicles for drug delivery." Journal of Pharmacy and Pharmacology, 1998; 50(5): 453-458.
47. Kauscher U, Holme MN, Björnmalm M, Stevens MM. Physical stimuli-responsive vesicles in drug delivery: Beyond liposomes and polymersomes. Adv Drug Deliv Rev., 2019; 138: 259-275. Doi: 10.1016/j.addr.2018.10.012
48. Chen S, Hao X, Liang X, Zhang Q, Zhang C, Zhou G, Shen S, Jia G, Zhang J. Inorganic Nanomaterials as Carriers for Drug Delivery. J Biomed Nanotechnol., 2016 Jan; 12(1): 1-27. doi: 10.1166/jbn.2016.2122. PMID: 27301169.
49. Paul, Willi, and Chandra P. Sharma. "Inorganic nanoparticles for targeted drug delivery." Biointegration of medical implant materials, 2020; 333-373.
50. Georgeous, Joel, Nour AlSawaftah, Waad H. Abuwatfa, and Ghaleb A. Husseini. "Review of gold nanoparticles: synthesis, properties, shapes, cellular uptake, targeting, release mechanisms and applications in drug delivery and therapy." Pharmaceutics, 2024; 16(10): 1332.
51. Zhuang, Wan-Ru, Yi Wang, Peng-Fei Cui, Lei Xing, Jaiwoo Lee, Dongyoon Kim, Hu-Lin Jiang, and Yu-Kyoung Oh. "Applications of π-π stacking interactions in the design of drug-delivery systems." Journal of Controlled Release, 2019; 294: 311-326.
52. Chorny, Michael et al. “Magnetically targeted delivery of therapeutic agents to injured blood vessels for prevention of in-stent restenosis.” Methodist DeBakey cardiovascular journal, 2012; 8(1): 23-7. doi:10.14797/mdcj-8-1-23
53. Peng, Shan, Yahua Wang, Na Li, and Chong Li. "Enhanced cellular uptake and tumour penetration of nanoparticles by imprinting the “hidden” part of

membrane receptors for targeted drug delivery." Chemical Communications, 2017; 53(81): 11114-11117.
54. Yilmaz, Eylul Gulsen et al. “A Sustainable Solution to Skin Diseases: Ecofriendly Transdermal Patches.” Pharmaceutics, 8 Feb. 2023; 15(2): 579. doi:10.3390/pharmaceutics15020579
55. Santos, Lúcia F et al. “Biomaterials for drug delivery patches.” European journal of pharmaceutical sciences: official journal of the European Federation for Pharmaceutical Sciences, 2018; 118: 49-66. doi: 10.1016/j.ejps.2018.03.020
56. Modrák, Marcel et al. “Biodegradable Materials for Tissue Engineering: Development, Classification and Current Applications.” Journal of functional biomaterials, 16 Mar. 2023; 14(3): 159, doi:10.3390/jfb14030159
57. Almoshari, Yosif. “Osmotic Pump Drug Delivery Systems-A Comprehensive Review.” Pharmaceuticals (Basel, Switzerland), 18 Nov. 2022; 15(11): 1430, doi:10.3390/ph15111430
58. Jeong, Woo Yeup et al. “Recent advances in transdermal drug delivery systems: a review.” Biomaterials research, 28 Jul. 2021; 25(1): 24, doi:10.1186/s40824-021-00226-6
59. He, Jiahui et al. “Wearable patches for transdermal drug delivery.” Acta Pharmaceutica Sinica. B., 2023; 13(6): 2298-2309. doi: 10.1016/j.apsb.2023.05.009
60. Nwagwu, Chibueze D., Amanda V. Immidisetti, Michael Y. Jiang, Oluwasegun Adeagbo, David C. Adamson, and Anne-Marie Carbonell. "Convection Enhanced Delivery in the Setting of High-Grade Gliomas" Pharmaceutics, 2021; 13(4): 561. https://doi.org/10.3390/pharmaceutics13040561
61. Ung, Timothy H et al. “Convection-enhanced delivery for glioblastoma: targeted delivery of antitumor therapeutics.” CNS Oncology, 2015; 4(4): 225-34. doi:10.2217/cns.15.12
62. Wang, Yucai et al. “Stimuli-Responsive Materials for Controlled Release of Theranostic Agents.” Advanced functional materials, 2014; 24(27): 4206-4220. doi:10.1002/adfm.201400279
63. Sheng, Yan et al. “Stimuli-responsive Carriers for Controlled Intracellular Drug Release.” Current medicinal chemistry, 2019; 26(13): 2377-2388. doi:10.2174/0929867324666170830102409
64. Lin, Xueqi et al. “Intellective and stimuli-responsive drug delivery systems in eyes.” International Journal of Pharmaceutics, 2021; 602: 120591. doi: 10.1016/j.ijpharm.2021.120591
65. Liu, Mengrui et al. “Internal stimuli-responsive nanocarriers for drug delivery: Design strategies and applications.” Materials science & engineering. C, Materials for biological applications, 2017; 71: 1267-1280. doi: 10.1016/j.msec.2016.11.030
66. Wang, Tianshuai, Chen Wu, Yanggen Hu, Yan Zhang, and Junkai Ma. "Stimuli-responsive nanocarrier delivery systems for Pt-based antitumor complexes: a review." RSC advances, 2023; 13(24): 16488-16511.
67. Hu, Huiyang, Prabhakar Busa, Yue Zhao, and Chao Zhao. "Externally triggered drug delivery systems." Smart Materials in Medicine, 2024; 5(3): 386-408.
68. Juthi, A. Z., F. Li, B. Wang, M. M. Alam, M. E. Talukder, and B. Qiu. pH-Responsive Super-Porous Hybrid Hydrogels for Gastroretentive Controlled-Release Drug Delivery. Pharmaceutics, 2023; 15(816): 2023.
69. Ferrero, Carmen, Marta Casas, and Isidoro Caraballo. "Redox-Responsive Polymersomes as Smart Doxorubicin Delivery Systems." Pharmaceutics, 2022; 14(8): 1724.
70. Meng, Xuan, Yongli Shen, Huanyu Zhao, Xinlei Lu, Zheng Wang, and Yanjun Zhao. "Redox-manipulating nanocarriers for anticancer drug delivery: a systematic review." Journal of Nanobiotechnology, 2024; 22(1): 587.
71. Dolui, Subrata, Bhanendra Sahu, and Sanjib Banerjee. "Stimuli-Responsive Functional Polymeric Materials: Recent Advances and Future Perspectives." Macromolecular Chemistry and Physics, 2025; 2400472.
72. Gaddimath, Shivalingayya, Shivanand Payamalle, Keshavananada Prabhu Channabasavana Hundi Puttaningaiah, and Jaehyun Hur. "Recent advances in pH and redox responsive polymer nanocomposites for cancer therapy." Journal of Composites Science, 2024; 8(1): 28.
73. Kopoleva, Elena, Maksim D. Lebedev, Alisa Postovalova, Anna Rogova, Landysh Fatkhutdinova, Olga Epifanovskaya, Alexander A. Goncharenko et al. "One-Pot Synthesis of Affordable Redox-Responsive Drug Delivery System Based on Trithiocyanuric Acid Nanoparticles." Nano Letters, 2023; 23(23): 10811-10820.
74. Liu, Zhe, Dong Zhou, and Lan Liao. "pH/Redox/Lysozyme-sensitive hybrid nanocarriers with transformable size for multistage drug delivery." Frontiers in Bioengineering and Biotechnology, 2022; 10: 882308.
75. Rodriguez-Devora, Jorge I et al. “Physically facilitating drug-delivery systems.” Therapeutic delivery, 2012; 3(1): 125-39. doi:10.4155/tde.11.137
76. Guillot, Antonio José et al. “Microneedle-Based Delivery: An Overview of Current Applications and Trends.” Pharmaceutics, 19 Jun. 2020; 12(6): 569. doi:10.3390/pharmaceutics12060569
77. Aldawood, Faisal Khaled et al. “A Comprehensive Review of Microneedles: Types, Materials, Processes, Characterisations and Applications.” Polymers, 22 Aug. 2021; 13(16): 2815, doi:10.3390/polym13162815
78. Chudzińska, Jagoda et al. “Microneedles Based on a Biodegradable Polymer-Hyaluronic Acid.” Polymers, 14 May. 2024; 16(10): 1396. doi:10.3390/polym16101396
79. Maia, R.F., Machado, P., Rodrigues, R.O. et al. Recent advances and perspectives of Microneedles

for biomedical applications. Biophys Rev., 2025; 17: 909–928. https://doi.org/10.1007/s12551-025-01317-7
80. Huang, Xiaoqi, Qiang Chang, Jian-hua Gao, and Feng Lu. "Sustained release microneedles: materials and applications in facial rejuvenation." Tissue Engineering Part B: Reviews, 2023; 29(3): 190-202.
81. Tucak, Amina et al. "Microneedles: Characteristics, Materials, Production Methods and Commercial Development." Micromachines, 27 Oct. 2020; 11(11): 961. doi:10.3390/mi11110961
82. Mohite, Popat et al. "Hydrogel-Forming Microneedles in the Management of Dermal Disorders Through a Non-Invasive Process: A Review." Gels (Basel, Switzerland), 7 Nov. 2024; 10(11): 719. doi:10.3390/gels10110719
83. Wilkes, Denise. "Programmable intrathecal pumps for the management of chronic pain: recommendations for improved efficiency." Journal of Pain Research, 3 Oct. 2014; 7: 571-7. doi:10.2147/JPR.S46929
84. Wesemann, Kelly et al. "Clinical accuracy and safety using the SynchroMed II intrathecal drug infusion pump." Regional anaesthesia and pain medicine, 2014; 39(4): 341-6. doi:10.1097/AAP.0000000000000107
85. Belverud, Shawn, Alon Mogilner, and Michael Schulder. "Intrathecal pumps." Neurotherapeutics, 2008; 5(1): 114-122.
86. Joung, Yeun-Ho. "Development of implantable medical devices: from an engineering perspective." International neurourology journal, 2013; 17(3): 98-106. doi:10.5213/inj.2013.17.3.98
87. Meng, Ellis, and Tuan Hoang. "MEMS-enabled implantable drug infusion pumps for laboratory animal research, preclinical, and clinical applications." Advanced drug delivery reviews, 2012; 64(14): 1628-38. doi: 10.1016/j.addr.2012.08.006
88. Pons-Faudoa, Fernanda P et al. "Advanced implantable drug delivery technologies: transforming the clinical landscape of therapeutics for chronic diseases." Biomedical microdevices, 18 May. 2019; 21(2): 47. doi:10.1007/s10544-019-0389-6
89. Del Bono, Fabiana, Nicola Di Trani, Danilo Demarchi, Alessandro Grattoni, and Paolo Motto Ros. "Active implantable drug delivery systems: engineering factors, challenges, opportunities." Lab on a Chip (2025).
90. Nandam N, Thung S, Venkatesh KK, Gabbe S, Ma J, Peng J, Dungan K, Buschur EO. Tandem T: Slim X2 Insulin Pump Use in Clinical Practice Among Pregnant Individuals with Type 1 Diabetes: A Retrospective Observational Cohort Study. Cureus., 2024 Jan 16; 16(1): e52369. doi: 10.7759/cureus 52369. PMID: 38361690; PMCID: PMC10868538.
91. Thrasher, James R., Arcelia Arrieta, Fang Niu, Katherine R. Cameron, Toni L. Cordero, John Shin, Andrew S. Rhinehart, and Robert A. Vigersky. "Early real-world performance of the MiniMed™ 780G advanced hybrid closed-loop system and recommended settings use in the United States." Diabetes Technology & Therapeutics, 2024; 26(S3): 24-31.
92. Djupesland, P.G. Nasal drug delivery devices: characteristics and performance in a clinical perspective—a review. Drug Deliv. and Transl. Res., 2013; 3: 42–62. https://doi.org/10.1007/s13346-012-0108-9
93. Liu Y, Wu D. Bi-directional nasal drug delivery systems: A scoping review of nasal particle deposition patterns and clinical application. Laryngoscope Investig Otolaryngol., 2023 Nov 22; 8(6): 1484-1499. doi: 10.1002/lio2.1190. PMID: 38130248; PMCID: PMC10731484.
94. Djupesland, P.G. Nasal drug delivery devices: characteristics and performance in a clinical perspective—a review. Drug Deliv. and Transl. Res., 2013; 3: 42–62. https://doi.org/10.1007/s13346-012-0108-9
95. Dighe, Sayali, Sunil Jog, Munira Momin, Sujata Sawarkar, and Abdelwahab Omri. "Intranasal drug delivery by nanotechnology: advances in and challenges for Alzheimer's disease management." Pharmaceutics, 2023; 16(1): 58.