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Recent Advances and Future Perspectives in Novel Drug Delivery Systems

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Abstract:

The effectiveness of pharmacotherapy depends not only on the drug molecule's pharmacodynamic and pharmacokinetic properties, but also on how well it is delivered to the target site at the therapeutic concentrations. Conventional dosage forms often pose significant obstacles, such as insignificant solubility, inadequate absorption, quick systemic elimination, absence of target specificity, and dose-dependent adverse effects. These issues are especially undesirable for drugs that are not effective well in small doses, fails to readily travel through membranes, or are easily metabolized by enzymes. Also, the fact that conventional formulations need patients to consume their medications more often may render them less likely to adhere to their regimens, which can make the therapy less effective. When consuming a drug by ingestion, the liver metabolizes the drug down first, which lowers the amount of the active ingredient in the blood. Novel Drug Delivery Systems (NDDS) were created to solve these significant problems. NDDS make it possible to regulate, maintain, or optimize drug release, which maximizes the benefits of drugs and minimizes their side effects. Nanoparticles, liposomes, microspheres, transdermal patches, implants, dendrimers, and microneedles are among the many of the technologies that have worked very well in clinical practice over the past few decades. These systems are frequently utilized to treat cancer, diabetes, neurology, and to give vaccines. One example is the mRNA-based COVID-19 vaccines. NDDS constantly encounters problems, like high development costs, complicated regulatory requirements, stability issues, and trouble in scaling up. But NDDS continue to evolve significantly with contribution of nanotechnology, biotechnology, and artificial intelligence. This comprehensive review article addresses about various types of NDDS, how they perform, their benefits and drawbacks, and potential future development in modern medicine.

Keywords: Novel Drug Delivery Systems, liposome, nanoparticles, controlled release, targeted therapy.

Introduction:

The primary objective of pharmacotherapy is to achieve a targeted therapeutic response while reducing adverse effects; however, this goal is often damaged by the biopharmaceutical limitations of drug

molecules rather than a lack of therapeutic potency. Several existing and newly discovered candidates suffer from inadequate clinical performance due to low water solubility, limited membrane

permeability, physiological instability, and high systemic clearance. Whereas conventional dosage forms like tablets and injections are cost effective, they often fail to overcome these challenges, resulting in variable plasma concentration of drug and increased risks of toxicity.

While oral administration remains the preferred route due to patient compliance, it is intrinsically controlled by physiological barriers, such as acidic gastric environments, enzymatic metabolism in the gastrointestinal tract, and high first-pass hepatic metabolism. Similarly, while parenteral administration bypasses first-pass metabolism, it brings challenges such as penetrativeness, risk of infection, and reduced suitability for chronic therapy. These limitations have become more noticeable with the development of advanced therapeutics such as peptides, proteins, nucleic acids, and monoclonal antibodies which are highly sensitive to environmental conditions and necessitate precise regulation of release and cellular uptake. Therefore, pharmaceutical research has focused on drug discovery toward the engineering of innovative delivery systems designed to optimized the potential of these complex molecules(1). NDDS indicates a significant framework shift by focusing on the maximization of drug disposition rather than the potency. By combining advances in nanotechnology, polymer chemistry, and biotechnology, NDDS can control the rate, duration of drug release, thereby maintaining therapeutic levels while reducing systemic exposure. These systems safeguard pharmaceutical products from environmental conditions and provide site specific drug delivery. The clinical effect of these technologies is proved better by the success of lipid nanoparticle-based mRNA vaccines, liposomal anticancer formulations, and long-acting injectable. Current NDDS platforms range from microscopic carriers like liposomes, niosome and dendrimers to

macroscopic systems such as transdermal patches and stimuli-responsive hydrogels.

Despite these advancements, the transition from lab-scale production to pharmaceutical application is filled with problems. Some crucial problems like large-scale manufacturing process, long-term stability problem, and high costs of development. Furthermore, the potential toxicity and biodistribution of novel nanomaterials required rigorous preclinical evaluation and robust regulatory oversight. Agencies increasingly need detailed characterization and risk-based development approaches, such as Quality-by-Design, to ensure quality safety and efficacy of drug.

In light of these complexities, a balanced Assessment is necessary to determine the suitability of NDDS on a case-by-case basis, considering therapeutic goals, patient requirement, and manufacturing feasibility(2). This review shows a comprehensive analysis of the evolution, design principles, and therapeutic applications of these systems. Furthermore, it probes the future of the field and highlights the key features of artificial intelligence (AI)-driven formulation design, personalized drug delivery, and smart, stimuli-responsive systems in redefining the landscape of modern pharmaceutical therapy.

Historical Background of NDDS

The history of drug delivery is the story of how we went from giving drugs in simple chemical forms to using complex molecular engineering to make them work more effectively with the human body. This change demonstrates that a growing number of individuals understand that a treatment's efficacy often depends less on how potent the drug is and more on how it transports to the target site in the body.

In the middle of the 20th century, the main goal was practical. Researchers attempted to render patients more likely to follow the regimen by developing oral dosage forms that released the drug slowly over time, which would extend the drug's therapeutic effects and make it easier for patients to administer their medicine. However, as the problems with traditional medicines and injections, like fluctuating plasma levels and systemic toxicity, became apparent, scientists continued to look for answers that were more precise.

The introduction of carrier-based systems like liposomes and nanoparticles in the 1970s and 1980s was an important milestone toward protection and stability. These carriers were important for protecting "delicate" complex drugs, such as proteins and peptides, from the body's hostile internal environment. By the 1990s, these novel concepts had reached clinical maturity with the use of transdermal patches and implantable systems, which gave healthcare professionals more control over how to treat chronic illnesses in chronic conditions.

The 21st century is marked by the integration of biotechnology and nanotechnology. We are no longer only giving out medicine; we are also using "smart" carriers like stimuli-responsive hydrogels, dendrimers, and microneedles that can interact with biological systems on a cellular level. The COVID-19 pandemic showed how effective this change was through rapidly introducing lipid nanoparticle-based mRNA vaccines. This showed that these multifaceted NDDS are now essential to world healthcare. The focus continues to lie on personalised medicine and AI-driven concepts as we proceed forward. This will assist in making sure that the next generation of delivery systems is as unique as the patients they treat(1,2).

Need and Objectives of NDDS(3–5)

The driving force behind NDDS is the identity that even the most potent drug molecule is ineffective if it cannot successfully handle the body's complex biological landscape. While conventional dosage forms like tablet and capsule are center to medicine, they often faced biopharmaceutical challenges such as low water solubility, limited membrane permeability, and high systemic clearance. For patient, these drawbacks manifest as unpredictable treatment outcomes, the need for frequent dosing, or the burden of invasive injections.

The need for NDDS has become even more critical with the rise of advanced therapeutics, including peptides, proteins, and nucleic acids. These "fragile" molecules are highly sensitive to their environment and sometimes cannot survive the body's natural defenses—such as harsh gastric acidity or first-pass hepatic metabolism without a sophisticated delivery vehicle. Consequently, the focus of pharmaceutical science is shifting from merely discovering new drugs to engineering intelligent systems that maximize the potential of the therapies we already have.

The primary objectives guiding NDDS research are centered on precision and protection:

Programmable Release and Protection:

Researchers goal to design carriers that protect drugs from environmental degradation while controlling the rate and duration of release whether immediate, sustained, or pulsatile to keep drug levels within a safe therapeutic window.

Site-Specific Targeting: By using nanotechnology and materials science, NDDS can be "programmed" for cell-specific targeting, ensuring the drug is directly delivered to the target site while sparing healthy tissues from off-target toxicity.

Biocompatibility and Innovation: A key goal is to ensure that these delivery systems are both biocompatible and biodegradable, reduce any long-term impact on the patient's physiology. Looking forward, the ultimate objective is to move toward personalized medicine. By integrating artificial intelligence (AI) and stimuli-responsive technologies, we are creating a future where drug delivery is no longer "one-size-fits-all" but is instead tailored to the unique biological needs of the individual(1,6,7).

Advantages and Limitations of NDDS(6,8)

NDDS is a revolutionary change in the field of pharmaceuticals because it avoids investigating stronger molecules and rather looks at how to effectively utilize drugs in the body. NDDS can help treatments succeed by emphasizing when, where, and how a drug is released. This helps the body perform more efficiently with its regular rhythms and reduces the adverse effects.

The most beneficial aspect about NDDS is that they may retain plasma drug levels in a narrow therapeutic window for a long time. This eliminates the detrimental "peaks and valleys" experienced when medicine was administered regularly. NDDS uses novel components like liposomes, polymeric nanoparticles, and hydrogels that respond to stimuli to preserve sensitive pharmaceuticals like peptides and nucleic acids from degradation in severe physiological settings. In addition, NDDS can be made to target certain cells or areas, which means that the medicine can travel to where it is required without affecting healthy tissues. This ability is especially useful for treatments that need to get through complex biological membranes or deal with drugs that do not dissolve well in water.

There are many problems that arise when trying to transform a successful lab prototype into a treatment in clinics. NDDS

have clear benefits, but they are often considered against significant practical and economic challenges. These novel drug delivery vehicles are often very complicated, and it's hard to manufacture in large scale and make sure that each batch is the same.

Many novel drug delivery systems, especially nanocarriers, have difficulties in remaining stable physically and chemically for a long-time during storage and transport. these problems combine with the high cost of development, limit their accessibility compared to simpler, more economical traditional dosage forms.

NDDS interact at molecular level in the biological system, therefore, there are ongoing concerns regarding the long-term safety and biodistribution of novel nanomaterials. As a result, regulatory bodies demand exhaustive characterization and risk-based development approaches, such as Quality-by-Design, to ensure that both the drug and its carrier are safe for human use.

Finally, NDDS should not be observed as a universally superior alternative for conventional drug delivery systems, but as a specialized toolkit that must be applied on a case-by-case basis. A fair evaluation is needed, taking into account the therapeutic goals and patient need as well as the realities of manufacturing feasibility and regulatory limits. This critical review can help us get to a future where drug delivery is not only effective, but also truly tailored to each patient(3).

Classification and Types of NDDS(3,9,10)

Novel drug delivery systems can be categorized based on therapeutic classification of drug loaded, physical form, intended application route of drug administration, and mechanism of action. (Table1). Major categories include Nanoparticle-based systems, Microparticle-based systems, Transdermal systems,

Implantable systems, Targeted systems, and other specialized carriers such as hydrogels,

pulmonary delivery systems, and ocular carriers (Figure 1).

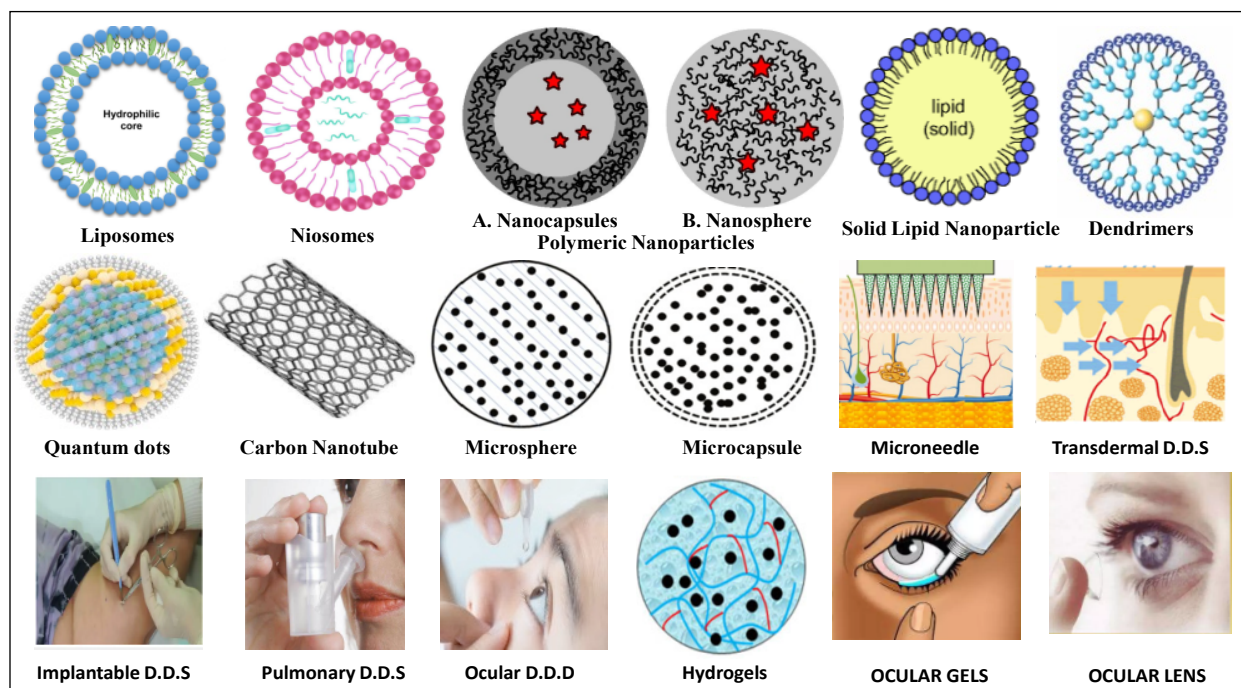


Figure 1: Novel Drug Delivery Systems

Table1: Classification, Examples and Clinical Relevance of NDDS:

NDDS Category	Representative Carriers	Example Drugs	Market/Clinical product	Key Advantages	Major Limitations
Liposome	Phospholipid Bilayer vesicles	Doxorubicin, Amphotericin B	Doxil, AmBisome®.	Increased biocompatibility, reduced systemic toxicity, enhanced circulation time	Physical and chemical instability, high production cost
Niosomes	Non-ionic surfactant vesicles	Acyclovir, Paclitaxel, Insulin	lancome cream, benzoyl peroxide gel	Cost-effective, improved stability compared to liposomes	Cost-effective, improved stability compared to liposomes
Polymeric Nanoparticle	PLGA, chitosan, PEGylated polymers	Paclitaxel, Risperidone	Abraxane®, Risperdal Consta®	Controlled drug release, improved targeting, BBB penetration	Complex manufacturing, regulatory hurdles

Solid-lipid Nanoparticle (SLN)	Solid lipid matrix	Antifungal, anticancer drugs	SLN-based topical formulations	High safety profile, good physical stability	Limited drug loading, drug expulsion during storage
Dendrimers	Highly balanced synthetic polymers	Anticancer drugs, siRNA	VivaGel®, SuperFect®	High loading efficiency, precise molecular architecture	Synthesis complexity, dose dependent cytotoxicity
Microparticles	Microspheres, microcapsules	Leuprolide acetate, vaccine	Lupron Depot®	Reduced dosing frequency, long-acting drug release	Invasiveness, injection site reactions
Transdermal systems (TDDS)	Patches, microneedles	Nicotine, fentanyl	Nicoderm®, Duragesic®	Sustained plasma level, non-invasive delivery	Limited drug permeability, skin irritation
Implantable systems (IDDS)	Biodegradable and non-biodegradable implants	Hormonal, Chemotherapy, carmustine	Norplant®, Gliadel® wafer	Prolonged localized drug delivery	Patient discomfort, surgical intervention
Pulmonary drug delivery system (PDDS)	Inhalers, nanoaerosols	Insulin, Salbutamol	Exubera®, Ventolin®	Avoidance of first-pass metabolism, rapid onset of action	Device dependency, dose variability
Ocular drug delivery system (ODDS)	Nanoparticles, inserts	Pilocarpine	Ocusert®	Prolonged ocular residence time	Formulation complexity, patient discomfort

Nanoparticle-based Systems(11–13)

Nanoparticles are small colloidal carriers, having particle size range of 10-200 nm, though they may increase up to 1000 nm. They are formulated using natural, synthetic, or semi-synthetic polymers as poly lactic-co-glycolic acid (PLGA), chitosan, gelatin, and albumin. Nanoparticles encapsulate hydrophilic or lipophilic drugs through adsorption or dispersion in a polymer matrix. Nanoparticles are further classified as:

Liposomes

Liposomes are spherical vesicles made up of one or more phospholipids bilayers which surround an aqueous core. The hydrophobic or lipophilic molecules are inserted into the bilayer membrane whereas hydrophilic molecules can be entrapped in aqueous core. Liposomes prevent drugs degradation, improve absorption, and give site specific delivery, commonly attained by linking ligands or antibodies to recognize particular receptors on cancer cells(14).

Market Products and Research

- Liposomal technology pioneered the successful delivery of mRNA COVID-19 vaccines by Pfizer-BioNTech and Moderna(15).
- **Doxil®** (doxorubicin loaded liposome) (Figure 2) is utilized in treatment of ovarian cancer and Kaposi's sarcoma, helping to diminish the side effects of the drug(16,17).
- **AmBisome®** (Amphotericin B loaded liposome) treats severe fungal infections with fewer side effects than traditional methods(18).
- **Marqibo®** (a liposomal vincristine) is used to treat specific form of leukemia. It improves the stability and efficacy of the medicine(19).
- **Depocyt®** (liposomal cytarabine) allows the sustained release of drug in cerebrospinal fluid for treating meningeal leukemia and lymphomatous meningitis(20,21).



Figure 2: Marketed Novel Drug Delivery Systems

Niosomes

Niosomes are non-ionic surfactants vesicles that are generally more stable, cheaper, and easier to prepare compared to liposomes. They have high encapsulation efficiency and are highly versatile for both oral and topical applications(22–24).

Niosomes of *Garcinia mangostana* extract were studied for enhanced stability and therapeutic efficacy against infections caused by *Acanthamoeba* species(25). There are some market products of niosomes available in the market as follows:

Market Products and Research

- Niosomes formulated by non-ionic surfactants and cholesterol showcase high stability, compatibility, and cost-effectiveness(26).

- Research has focused on pH-responsive niosomes for delivering paclitaxel in cancer therapy.
- Niosomes-based market products include Anti-Aging Creams (e.g. Lancome cream)(Figure 2)(27), Acne Treatment Gel(e.g. benzoyl peroxide gel IP)(28), and Hair Growth Solutions (e.g. pumpkin seed oil niosome which improve absorption(29,30)).

Polymeric Nanoparticles

These nanoparticles are formulated by using biodegradable polymers (ex- PLGA, chitosan, polylactide) and act as controlled-release carriers. They are used to carry anticancer drugs like paclitaxel. Crucially, they are helpful in brain targeting because

they can cross the BBB, allowing drugs to reach in the brain effectively(31–35).

Market Products:

- **Abraxane®:** Albumin bound paclitaxel nanoparticles employed in treatment of breast, lung, and pancreatic cancer treatment, which helps the drug reach cancer cells better and reduces harmful side effects compared to conventional formulations (Figure 2)(36).
- **Eligard®:** It is an Androgen suppression therapy that decrease testosterone levels, inhibit growth of prostate cancer. These biodegradable polymeric nanoparticles release the drug slowly for prolonged period of time and decrease the need for repeated injections(37).
- **Sandostatin LAR®:** This is used for acromegaly and certain tumors. The polymeric nanoparticles slowly release octreotide, giving long-lasting effects with fewer doses(38).
- **Risperdal Consta®:** Polymer-based nanoparticles provide a slow and steady release of risperidone for schizophrenia and bipolar disorder, reducing the need for frequent dosing(39,40).

Solid Lipid Nanoparticles (SLN)

SLN are formulated by using solid lipids, stabilized with surfactants, merging the benefits of liposomes and polymeric nanoparticles. They offer high drug stability and provide controlled release of the drug. The materials used are generally biodegradable and biocompatible, making them useful for carrying anticancer drugs, antifungal drugs, and vaccines(41,42).

Market Products

- **Cutanova Cream Nano Repair Q10:** The first SLN product (Figure 2) commercially released (October 2005), delivering coenzyme Q10 for anti-ageing and skin repair(43).

- **NLC Deep Effect Eye Serum:** Uses nanostructured lipid carriers for moisturizing and anti-wrinkle benefits(44–46).

Dendrimers

Dendrimers are highly branched, treelike macromolecules where drugs entrapped in their cavities or attached to their surface, allowing precise drug targeting. They are used for gene delivery (DNA or RNA) and play an important role in anticancer therapy(47–50).

Market Products

- **VivaGel®:** A vaginal gel used for the treatment of sexually transmitted disease as HIV and herpes simplex virus (Figure 2). It is one of the first dendrimer medicines approved for human use.(51).
- **SuperFect® and Prioject®:** Commercial dendrimer products used in research laboratories for transferring DNA into cells (transfection reagents)(52,53).

Quantum dots

Quantum dots are small semiconductor crystals having special optical qualities, mostly used to capture images and track drugs inside the body due to their bright fluorescence. They are merged with drugs or ligands so that medicines reach specific tissues, making them useful for both diagnosis and therapy (theranostics)(54–56).

Market Products

- **EviDots®:** Quantum dots made for bio-labeling and sensing in research and clinical diagnostics, offering high brightness and stability for tracing drugs and disease cells(57).
- **Qdot™ Nanocrystals:** These quantum dot kit available for medical and research tracing, used in delivery and imaging of nanoparticles in cells and tissues(54).

Carbon Nanotubes (CNTs)

CNTs have hollow cylindrical structure with a high surface area that can cross cell membranes. They can deliver drugs, genes, or proteins inside their hollow core or attached to their surface. Due to their small size, they reach difficult areas like tumors and brain. Research explores their use for cancer treatment, genetic delivery, and vaccine transport. CNTs deliver drugs in a controlled manner and sometimes even respond to external triggers like light or heat. Their safety and long-term effects are still under research, because carbon-based materials may cause toxicity if not properly modified(58–60).

Market Products

- **Arkema Graphistrength® CNTs:** They are Used in NDDS and research for coating tablets, capsules and creating biosensors for medicine monitoring (Figure 2)(61).
- **Nanocyl NC7000® CNT Powders:** These are used for cancer therapy, gene therapy and imaging, with refined purity and functionalization options(62).

Microparticle-based Systems

Microparticle system incorporate drugs into micro-sized particle (1-1000 μm) to achieve controlled, sustained, or targeted release(63).

- **Microspheres:** A microsphere is a small, spherical polymer matrix particle where drug is uniformly dispersed.
- **Microcapsules:** A microcapsule is a reservoir type core shell particle where drug is enclosed in a central core and surrounded by a distinct polymer shell(64).

These systems protect drugs from enzymatic and chemical degradation, provide prolonged drug release, and are effective in pediatrics for masking the bitter taste of drugs. They are widely used in depot

injections for schizophrenia and hormonal therapy.

Market Products

- **Sandostatin LAR® (Octreotide microspheres)** uses biodegradable microspheres for slow drug release, lasting about four weeks with one injection(65).
- **Risperdal Consta® (Risperidone microspheres)** releases medicine gradually over two weeks for schizophrenia and bipolar disorder(66).
- **Decapeptyl SR® (Triptorelin microspheres)** (Figure 2) issued in management of prostate cancer, infertility-related problems, and endometriosis. The microspheres make the drug effective for weeks with a single dose(67).
- **Lupron Depot-PED® (Leuprolide acetate microspheres)** is formulated for children for treating central precocious puberty (early puberty), microspheres release medicine slowly to control early sexual development with fewer injections(68).

Transdermal Drug Delivery Systems (TDDS)

TDDS transport drugs into the bloodstream via skin by using special patches, bypassing the stomach or liver. This approach reduces side effects, avoids frequent dosing, and is painless, simple to use and improves patient comfort(69–71).

TDDS are mainly classified into two types:

- **Transdermal patches:** These are thin patches that stick to the skin and release medicine slowly over a long time. The drug passes through the skin and reaches the blood. They are painless, easy to use, and give controlled drug release(72).
- **Microneedles:** These are very tiny needles which make small, painless

holes in skin to improve absorption of larger drugs. Dr. Mark R. Prausnitz *et al.* developed microneedles for painless insulin delivery(73).

Market Products

- **Catapres-TTS® (Clonidine patch):** Used for the management of hypertension. The patch release drugs steady and controlled way for several days(74).
- **Nitro-Dur® (Nitroglycerin patch):** Used for preventing chest pain (angina) in patients with heart problems. The patch ensures a continuous supply of the drug and helps maintain blood flow to the heart(75).
- **Duragesic® (Fentanyl patch):** (Figure 2) Provides long-lasting relief for severe chronic pain, such as cancer pain. The patch provides long-lasting relief by releasing the drug slowly through the skin(76).
- **Exelon® Patch (Rivastigmine patch):** Delivers Rivastigmine continuously through the skin for treatment of Parkinson's disease dementia and Alzheimer disease(77).

Implantable drug delivery system (IDDS)

The implantable system for sustained drug release was introduced by Lafarge in 1861. These are devices which placed inside the body to achieved sustained, controlled, and targeted delivery for longer time(78,79).

Market Products

- **Norplant® (Levonorgestrel implant):** It is a set of small, flexible rods (Figure 2) implanted in the skin of the upper arm. They slowly releases levonorgestrel, a hormone that prevents pregnancy for up to 5 years(80).
- **Gliadel® Wafer (Carmustine implant):** It is a small biodegradable implant placed directly in the brain after

cancer surgery to remove a tumor. It slowly releases carmustine, a chemotherapy drug, to kill any remaining cancer cells(81).

- **Ozurdex® (Dexamethasone implant):** A small implant placed into the eye which releases dexamethasone, a corticosteroid, to treat swelling in the eye caused by diabetic macular edema or retinal vein occlusion(82).
- **Probuphine® (Buprenorphine implant):** It is a group of small rods which implanted under the skin of the arm. It delivers buprenorphine steadily for 6 months to help patients with opioid dependence, reducing cravings and withdrawal symptoms(83).

Pulmonary Drug Delivery Systems (PDDS)

PDDS is a method in which drugs are given through the lungs using inhalers or nebulizers. In this system, the drug is inhaled in the form of gas, mist, or very fine particles. Because lungs have large surface area and high blood supply, drugs quickly reach the bloodstream, offering faster action, reduced side effects, and requiring a smaller dose. Pulmonary delivery is painless, effective, and easy for patients to use. This system is very useful for treating lung diseases like asthma, COPD, and also for delivering some systemic drugs(84–86).

Market Products

- **Ventolin® Inhaler (Salbutamol/Albuterol):** It delivers salbutamol directly to the lungs for quick relief during asthma attacks (Figure 2)(87).
- **Advair Diskus® (Fluticasone + Salmeterol):** It is a dry powder inhaler that contains two medicines: fluticasone (steroid that diminish airway swelling) and salmeterol (bronchodilator keeps

airways open). It is employed in treatment asthma and COPD(88).

- **Spiriva® HandiHaler (Tiotropium):** It is an inhaler that delivers tiotropium, a bronchodilator. It is used mainly for COPD patients to help them breathe more easily by keeping their airways relaxed for a long time(89).
- **Pulmozyme® (Dornase alfa inhalation solution):** It is a nebulizer solution used mainly in patients with cystic fibrosis. It breaks down thick mucus in the lungs, making it easier to cough out and improving breathing(90).

Ocular Drug Delivery Systems (ODDS)

ODDS supply drugs into the eyes, aiming deliver the accurate amount of drug at the target site and maintain its effect for the management of different eye diseases like infections, dryness, inflammation, or glaucoma. The goals of this system are to deliver the right amount of drug at the right site and maintain its effect for a longer time. They overcome the poor bioavailability of traditional eye drops (due to tear drainage and blinking) using ocular inserts, nanoparticles, in-situ gels, and drug-loaded contact lenses(91,92).

Market Products

- **Ocusert® (Pilocarpine ocular insert):** It is a small eye insert that slowly releases pilocarpine into the eye. It is used for treating glaucoma, lasting about one week(93).
- **Retisert® (Fluocinolone acetonide implant):** It is a tiny implant placed inside the eye (Figure 2) which releases fluocinolone, a corticosteroid, for about 2-3 years. It is used to treat chronic disease like uveitis, a serious inflammation inside the eye(94).
- **Ozurdex® (Dexamethasone implant):** It is a biodegradable implant inserted into eye which releases dexamethasone

and reduce swelling (macular edema) caused by diabetes or retinal vein blockage(95).

- **Durysta® (Bimatoprost implant):** It is an implant inserted into the eye, releasing bimatoprost. It is used in management of glaucoma (an eye disease that increase eye pressure)(96).

Hydrogels

Hydrogels are three-dimensional polymers network that take up a high amount of water or biological fluids without dissolving. They are soft, biocompatible, and widely employed as carriers in the formulation of sustained and controlled release of drugs(97). Stimuli-sensitive hydrogels expand or contract in response to variation in pH, temperature, or other biological signals, making them ideal for targeted and smart drug delivery. Hydrogels act as guard for responsive molecules as peptides, protein and nucleic acids from degradation until they reach the target site(98–100).

Market Products

- **Juvéderm®:** A hydrogel made of hyaluronic acid, mainly used for cosmetic and medical applications like facial fillers and controlled drug delivery (Figure 2)(101).
- **Regranex® Gel:** It contains hydrogel carboxymethyl cellulose, used for treatment of wound healing, especially in diabetic ulcers(102).
- **Pluronic® F127:** it is a thermo-sensitive hydrogel (liquid at cool temperatures, converts to gel at body temperature)widely used for delivering nanoparticles in controlled release formulations(103).

Table 1 details the primary NDDS, detailing their carriers, the drugs they deliver, approved products, and their various pros and cons. This comparison highlights the wide variety of these platforms and shows

that their success in moving from the lab to the clinic varies significantly.

Applications of Novel Drug Delivery Systems

NDDS offer practical solutions to solve challenges of conventional drugs by improving targeting, systemic availability, patient compliance. NDDS have transformed the management of several chronic and serious diseases(1,6). The major areas of application include Cancer therapy, Diabetes management, Neurological disorders, Infectious diseases, Cardiovascular diseases, Ocular disorders, Vaccines, immunotherapy, Hormonal and reproductive health, pulmonary diseases, and Pain management.

NDDS in Cancer Therapy

NDDS make cancer treatment more effective and safer by supply drugs immediately to the tumor place without harming any normal tissue. Liposomes, nanoparticles, and niosomes give controlled and targeted delivery of anticancer drugs(104,105). Abraxane is a Nanoparticle-bound paclitaxel that improves drug delivery to cancer cells without using toxic solvents(36). Recent research developed pH-responsive niosomes for delivering paclitaxel, which have higher tumor-killing ability by releasing the drug when activated by the tumor's acidic environment(106).

NDDS in Diabetes Management

NDDS deliver medication in a safer, easier, and more effective way, improving upon traditional insulin injections which cause pain, low patient compliance, and fluctuations in blood sugar levels(107). Exubera was the first inhaled insulin allowed patients to take insulin without injections, and microneedle patches are now developed to deliver insulin painlessly through the skin(108). Recent advances of glucose-responsive nanoparticles that release insulin when blood sugar levels increase,

providing a smart and patient-friendly option for better control of diabetes. Studies also focus on oral insulin-loaded nanocapsules designed to survive in the stomach environment and deliver insulin directly to the intestine(109,110).

NDDS in Neurological Disorders

NDDS play a major role by overcoming the challenge of the BBB. They Supply drugs immediately to brain in controlled and targeted manner(111). Risperdal Consta contain risperidone for treatment of schizophrenia and helps in maintaining steady drug levels, reducing the frequency of dosing(112). Recently, the use of intranasal lipid nanoparticles carrying donepezil for Alzheimer's disease showed memory improvement and higher brain targeting compared to conventional drugs. These advancements propose that NDDS improve the effectiveness of drugs for management of disease like Parkinson's disease, Alzheimer's disease, epilepsy, and depression by increasing brain targeting, reducing side effects, and ensuring long-term release of drug, making them highly valuable in the management of neurological disorders(113).

NDDS in Infectious Diseases

NDDS improve the management of long-term treatments for infections like tuberculosis, HIV, and fungal diseases by supply drugs immediately to infected cells. NDDS, like liposomes, nanoparticles, and niosomes make therapy more effective by providing targeted delivery(114). AmBisome, amphotericin B loaded liposome, is used in cure of fungal infections with less kidney toxicity than the conventional drug(18). Recent research reported polymeric nanoparticles for malaria treatment, showing stronger action against resistant parasites. Such innovations highlight that NDDS can make infectious

disease management safer, more effective, and more patient-friendly.(115,116).

NDDS in Cardiovascular Diseases

NDDS are very helpful in controlling cardiovascular diseases by allowing targeted drug delivery immediately to blood vessels and heart, which improves effectiveness and reduces side effects of drugs. Traditional treatments often face problems like short half-life and low bioavailability, but NDDS such as nanoparticles, liposomes, and stents with drug coatings provide controlled and site-specific release(117). Drug-eluting stents release medicines like sirolimus or paclitaxel directly at the site of blocked arteries, preventing re-narrowing and reducing the need for repeat surgery(118). Research also shows that nanocarriers for delivering statins enhanced cholesterol-lowering effects and reduced inflammation in animal models. These advances make NDDS more precise, effective, and long-lasting, enhance patient compliance in the treatment of cardiovascular disease(119,120).

NDDS in Ocular Disorders

NDDS plays a major role in the management of ocular disorders as a result of increase the absorption of drug, prolonged drug action, and decrease the need for frequent dosing. NDDS such as liposomes, niosomes, nanoparticles, and in situ, deliver drugs directly into eye in controlled way(121). Niosomal formulations of timolol are used to control intraocular pressure in glaucoma compared to simple eye drops. Chitosan-coated nanomicelles used for sustained delivery of anti-glaucoma drugs, showing enhanced ocular retention and reduced side effects(122).

NDDS in Vaccines and Immunotherapy

NDDS increase the stability of vaccines and immunotherapy, by providing targeted delivery, in controlled and sustained

way(123). Liposomal formulations used for hepatitis A and influenza vaccines to improve efficacy(124). In immunotherapy, Nanoparticle-based carriers are being used, which deliver drugs directly to tumor sites, thereby enhance effectiveness and reduce the adverse effect(125). A current study highlighted the effectiveness of lipid nanoparticles in mRNA-based tumor vaccines, which demonstrated strong immune activation and improved tumor control. Thus, NDDS provides safer, more effective, and long-lasting options in modern vaccines and immunotherapy(126).

NDDS in Hormonal therapy and Reproductive Health

NDDS provide controlled and long-term release of hormones, reducing side effects and increasing patient compliance. Conventional hormonal therapies need frequent dosing, but NDDS such as implants, Transdermal patches, microspheres, and vaginal rings maintain a steady level of hormones(127). Vaginal ring (NuvaRing) releases etonogestrel and ethinyl estradiol for contraception over three weeks, while depot injections of leuprolide microspheres are used in reproductive disorders like endometriosis(128). Biodegradable polymer-based implants used for long-acting contraceptives, which have better safety and convenience for patients compared to daily pills. These advanced systems make hormonal therapy and reproductive health management more effective, patient-friendly, and reliable(129).

NDDS in Pulmonary Diseases

NDDS supply drugs immediately to the lungs, increasing drug absorption and reducing the adverse effects of drugs. They provide sustained release and better targeting of lung tissues(130). Liposomal formulations of budesonide employed in the cure of asthma(131), and nanoparticles-based inhalers used in the management of

COPD(132). Recently reported that polymeric nanoparticles used for tuberculosis management through inhalation, which showed higher lung retention and better patient outcomes. Thus, NDDS makes pulmonary therapy more effective, safe, and convenient for long-term disease management(133).

NDDS in Pain Management

NDDS give controlled and sustained delivery, while lowering the need of frequent dosing and minimizing side effects. Conventional painkillers can cause some problems like gastric irritation or short

duration of action, but NDDS such as transdermal patches, liposomes, and injectable microspheres increase the safety and effectiveness of the drug(134). Example includes fentanyl transdermal patch for cancer pain and liposomal bupivacaine for prolonged local anesthesia(135). Recent research focuses on the improvement of polymer-based nanocarriers for delivering NSAIDs to diminish pain while minimizing gastric toxicity(136).

The summary of application of NDDS is given in Table 2.

Table 2: Therapeutic Applications of Novel Drug Delivery Systems

Therapeutic Area	NDDS category	Product example	Clinical Advantage
Cancer therapy	Liposomes, polymeric nanoparticles	Doxil®, Abraxane®	Enhanced tumor targeting, reduced systemic toxicity
Diabetes mellitus	Pulmonary delivery, microneedles	Inhaled insulin formulations	Improved patient compliance, non-invasive delivery
Neurological disorders	Polymeric nanoparticles, implants	Risperdal Consta®	Sustained drug release, improved CNS bioavailability
Infectious diseases	Liposomes, nanoparticles	AmBisome®	Reduced organ toxicity, improved therapeutic index
Cardiovascular diseases	Drug-eluting stents	Sirolimus-eluting stents	Prevention of restenosis, localized drug action
Ocular disorders	Ocular inserts, implants	Ocusert®, Ozurdex®	Prolonged ocular residence time, reduced dosing
Vaccination	Lipid nanoparticles	mRNA-based COVID-19 vaccines	Enhanced antigen delivery and immune response
Pain management	Transdermal patches	Fentanyl patch	Sustained analgesia, improved adherence
Hormonal therapy	Microspheres	Lupron Depot®	Long-acting therapy, reduced dosing frequency
Pulmonary diseases	Inhalable nanoparticles	Salbutamol inhalers	Rapid onset of action, targeted lung delivery

Future Perspectives of Novel Drug Delivery Systems

The future of NDDS focused on technology integration, customisation, and accessibility

The advancements in genomics, proteomics, and metabolomics increase the development of drug delivery methods for individual patient needs, significantly lowering side effects and make treatment more effectiveness. The addition of Artificial Intelligence (AI) and machine learning increase improvement by Forecasting how drugs connect with carriers like liposome, niosome and optimizing Nanoparticle designs for specific targeting. Advanced stimuli-sensitive and smart delivery systems are being made to deliver drug only when activated by specific conditions like changes in temperature, Ph and ensuring precise

targeting and reducing drug wastage and side effects. Emerging technologies like 3D printing enhance production of modified drug formulations developed to satisfy unique patient requirements. Long-acting injectable and implantable devices will increase customer satisfaction by lowering the frequency of doses, particularly in long term disease care. A significant focus is on making NDDS affordable and accessible globally, particularly in low- and middle-income region, by simplifying manufacturing and developing formulations that are stable at room temperature (Table 3).

Table 3: Emerging trends and future directions in NDDS

Emerging Strategy	Description	Expected Impact on Drug Delivery
AI-driven formulation design	Use of machine learning and predictive modeling for carrier optimization	Reduced development time, precision formulation
Stimuli-responsive delivery systems	pH-, enzyme-, temperature- or redox-triggered drug release	Site-specific delivery, minimized off-target effects
Personalized NDDS	Patient-specific delivery platforms based on genetic and physiological profiling	Advancement of precision medicine
3D-printed drug delivery systems	Additive manufacturing of customized dosage forms	Flexible dosing, improved patient adherence
Long-acting injectable formulations	Sustained drug release over weeks to months	Reduced dosing frequency, better compliance
Thermostable NDDS	Formulations stable at room temperature	Improved global accessibility, especially in LMICs
Multifunctional nanocarriers	Combined targeting, imaging, and therapy (theranostics)	Enhanced treatment monitoring and efficacy
Gene and nucleic acid delivery systems	Carriers for siRNA, mRNA, CRISPR components	Treatment of genetic and complex diseases

The future prospects of NDDS are focused on providing safer, quicker, and more effective therapies that will transform healthcare from a uniform model to personalized and precision treatment, significantly increasing patient quality of life.

Conclusion

The progresses of NDDS make a major milestone in modern medicine by overcoming the limitation of conventional drug delivery system such as limited bioavailability and generalized toxicity. The

modern methods, including nanoparticles, liposomes, dendrimers, and microneedles, enable targeted and controlled drug release, hence increasing effectiveness and reducing the adverse effects of drugs. NDDS have obtained major effectiveness in controlling chronic diseases like cancer, neurological disorders, diabetes, and vaccine delivery, also including the recently developed mRNA COVID-19 vaccines. Although significant difficulties remain, including high costs of development, complex manufacturing processes, stability issues, and prolonged regulatory approvals, current research is actively addressing these challenges by using advanced technologies such as AI, biotechnology, and nanotechnology. The future of NDDS is strongly linked with the concept of personalized and precision medicine, where treatments can be adjusted tailored on an individual's genetic profile. Furthermore, smart and stimuli-responsive carriers are being designed to release drug in response to specific physiological triggers, provide extra precise and patient-friendly therapies. The addition of 3D printing technology grants the creation of customized drug formulations to fulfill individual patient needs. Long-acting injectable and implantable devices are also coming forward to provide customer satisfaction by lowering need of frequent dosing, particularly in long term disease treatment. A significant focus is on making NDDS more accessible and affordable globally by simplifying manufacturing and developing formulations that are stable at room temperature, which is particularly vital for low- and middle-income region. The addition of NDDS with regenerative medicine make promise for faster and more effective tissue repair and healing. NDDS have both scientific advancement and a practical and transformative solution for global health issues. As research and innovation continue, and cost barriers are

lowered, these advanced drug deliveries are predictable to become main stream in clinical practice, improving patient compliance and the quality of life worldwide.

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