Comparative Analysis of Novel Drug Delivery System for Various Disease

[1]Viraj Daunge, [2]Sahil Deshmukh, [3]Bhakti Dhage, [4]Vandana Shirsath, [5]Anil Jadhav
[1]Student
[1,2,3,4,5]Mahavir Institute of Pharmacy, Varvandi Road, Nashik, Maharashtra, India
[1]9322240861, daungeviraj@gmail.com

Abstract-This review provides a comprehensive comparative analysis of several novel drug delivery systems (NDDS), highlighting their applications across diverse diseases. Emphasis is placed on the latest advancements in nanoparticulate delivery platforms—including liposomes, tocosomes, hydrogels, microneedles, and nanobots—and their ability to overcome limitations of conventional dosage forms. The discussion encompasses critical aspects such as targeted drug delivery, controlled release, improved drug stability, and biocompatibility. NDDS technologies are shown to optimize therapeutic efficacy while minimizing toxicity, promote personalized and regenerative medicine, and facilitate advanced diagnostic and therapeutic methods. The challenges of poor bioavailability, rapid clearance, and limited biological distribution are addressed through engineering strategies, with particular focus on carrier types and their respective advantages and disadvantages. The review synthesizes current clinical evidence, recent drug examples, and ongoing translational challenges, positioning NDDS as pivotal drivers in modern medical treatments

Index Terms—Novel drug delivery systems, Nano pharmaceuticals, Liposomes, Tocosomes, Hydrogels, Microneedles, Nanobots, Targeted therapies, Controlled release, Biocompatibility

I. INTRODUCTION

Drug Delivery Systems (DDS) represent a promising technological advancement with extensive applications, engineered to release drugs in a controlled manner and at a predetermined rate while delivering them to specific tissues or cell types. Recent developments such as nanoparticles, molecularly imprinted polymers, and 3D printing technology have emerged as cutting-edge research topics in the field of drug innovation. Nano pharmaceuticals are specifically designed to precisely deliver drug substances to targeted tissues and cells, aiming to optimize therapeutic

efficacy while minimizing potential adverse effects. Novel drug delivery systems (NDDSs) can be utilized to enhance the performance of biotherapeutic agents compared to their conventional dosage forms [1]

The effectiveness of natural products in clinical trials has often been limited, with most pharmaceutical companies reluctant to pursue their development. This is primarily due to concerns regarding poor solubility, limited biological distribution, or rapid metabolic clearance, which may result in plasma drug concentrations falling below therapeutic levels. Additionally, permeability and absorption across biological membranes and barriers can be challenging for compounds with relatively high molecular weight and low lipophilicity, resulting in poor drug transport efficiency and short half-lives. Thus, identifying new drug delivery methods is crucial to address these issues. Research currently focuses on maximizing the efficacy of natural products, leading to the emergence of more innovative drugs with fewer side effects. [2]

Effective drug delivery systems are vital for maximizing medical treatments and patient benefits. By enabling drugs to reach targeted sites in the body, these systems significantly enhance therapeutic efficacy, resulting in improved treatment outcomes. Targeted drug delivery reduces exposure to off-target tissues, thus lowering toxicity and undesired side effects. Nano pharmaceuticals further enhance the ability to tailor treatments to specific disease profiles, supporting advances in personalized medicine and regenerative therapieses [3]

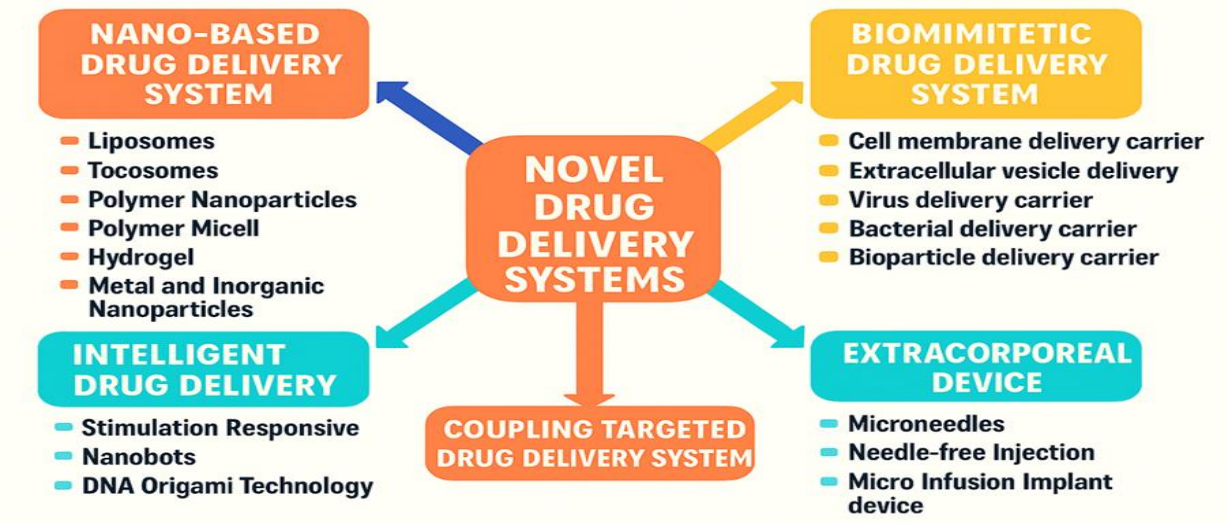
II. DISEASE DIAGNOSIS

Nanoparticle-based systems can aid in early and precise diagnosis of diseases.

- Targeted Therapy and Drug Delivery: NDDSs enhance the specificity of treatment, focusing drug action on diseased tissue and minimizing side effects.
- Personalized Medicine: Customizable drug carriers allow for individualized therapy, improving patient adherence and outcomes.
- Regenerative Medicine: Controlled release systems provide sustained delivery needed for tissue regeneration and healing.
- Safety and Efficacy: Advanced DDS reduces severe adverse effects and improves the overall quality of patient life. [4]

The key objective of designing NDDS is to help achieve an enhanced quality of patient life securely by avoiding or limiting drug abuse or severe adverse effects associated with traditional therapies. NDDS aim to elevate therapeutic outcomes by precise targeting, controlled drug release, and improving the pharmacological profile of biotherapeutic agents. [5]

Types of novel drug delivery systems (NDDS) [6]



LIPOSOME

Liposomes were firstly discovered in the 1960's by Bengham and later became among the most expansive drug delivery systems. Liposomes nanoemulsions are widely used nanoparticles in nanomedicine mainly due to their biocompatibility, stability, ease to synthesize and high drug loading efficiency, high bioavailability, and their safe excipients used in these formulations. due to their size, hydrophobic and hydrophilic characteristics and their ability toof cholesterol into liposomes is indispensable since cholesterol modulates membrane permeability, changes fluidity, and improves the stability of bilayer membranes in the presence of biological fluids such as blood and plasma. Liposomal formulations may also contain polymers, and even membrane protein to prolong their circulation half-life, improve the biodistribution profile and enhance the encapsulated drug effectiveness.

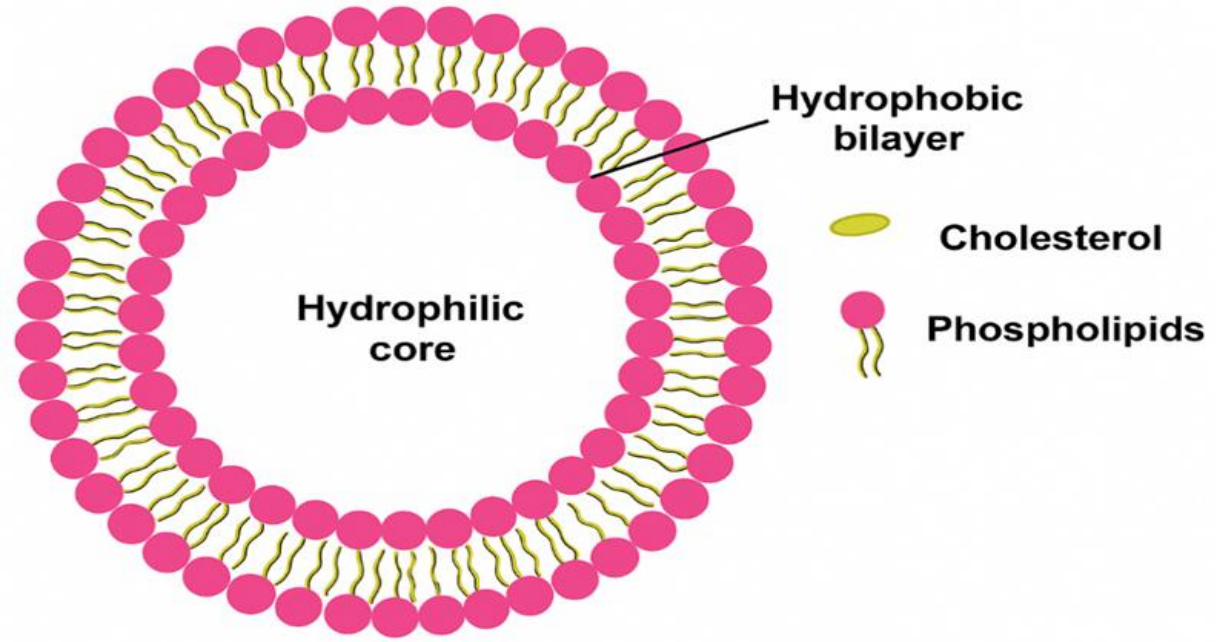


Figure 1 Liposome.

According to the liposomes structures, they are classified into four categories based on size and number of bilayers: small unilamellar vesicles (SUV), large unilamellar vesicles (LUV), multilamellar vesicle (MLV), [7]

ADVANTAGES

It offers targeted drug delivery
Increased efficacy and therapeutic index of drug
Liposome helps to reduce exposure of sensitive tissues to toxic drugs
Prevent oxidation of drugs
Liposomes are biodegradable
Liposome increases the stability of drug

DISADVANTAGES

Low solubility
Short half-life
Production cost is high
Leakage and fusion of encapsulated drug may occur
Allergic reactions may occur to liposomal constituents

LIST OF CLINICALLY APPROVED LIPOSOMAL DRUGS

Name	Trade Name	Company	Indication
Liposomal Amphotericin B	Abelcet	Enzon	Fungal infections
Liposomal Amphotericin B	Ambisome	Gilead Sciences	Fungal and protozoal infections
Liposomal Cytarabine	Depocyt	Pacira (Formerly Skye Pharma)	Malignant lymphomatous meningitis
Liposomal Daunorubicin	DaunoXome	Gilead Sciences	HIV-related Kaposi's sarcoma
Liposomal Doxorubicin	Myocet	Zeneus	Combination therapy with cyclophosphamide in metastatic breast cancer
Micellular Estradiol	Estrasorb	Novavax	Menopausal therapy
Vincristine	Onco TCS	–	Non-Hodgkin's lymphoma
Lurtotecan	NX211	–	Ovarian cancer
Nystatin	Nyotran	–	Topical antifungal agent
Liposomal Vaccine	Epaxal	Berna Biotech	Hepatitis A
Liposomal Vaccine	Inflexal V	Berna Biotech	Influenza
Liposomal Morphine	DepoDur	Skye Pharma, Endo	Postsurgical analgesia
Platinum Compounds	Platar	–	Solid tumours
DNA plasmid encoding HLA-B7 and α2 microglobulin	Allovectin-7	–	Metastatic melanoma

TOCOSOME

The development of novel nanocarrier systems for drug delivery is crucial for enhancing therapeutic efficacy and stability while minimizing toxicity. In this study, we explore the potential of α-tocopheryl phosphate (TP) and di-α-tocopheryl phosphate (T2P), two derivatives of vitamin E, as key components in tocosome-based drug delivery systems. Tocosomes were formulated using the Mozafari method, incorporating TP, T2P, and

various lipids/phospholipids, including phosphatidylcholine, stearyl amine, Phospholipon 90H, and Phospholipon 100H, with and without cholesterol

Tocosomes possess a number of important advantages when compared with other dispersed systems, including a high encapsulation of water-soluble and lipid-soluble compounds, cost effectiveness, and reproducible sustained release rates. Tocosomal formulations can replace some commercially available products containing toxic solubilizing agents. Therefore, they provide effective and safe alternative dosage forms for parenteral, intravenous, transdermal, and oral administration. Similarly, these vesicles can be used in the formulation of novel nutraceutical, food, and feed products since they provide improved ingredient stability, enhanced bioavailability, and controlled release of the encapsulated molecules [9]

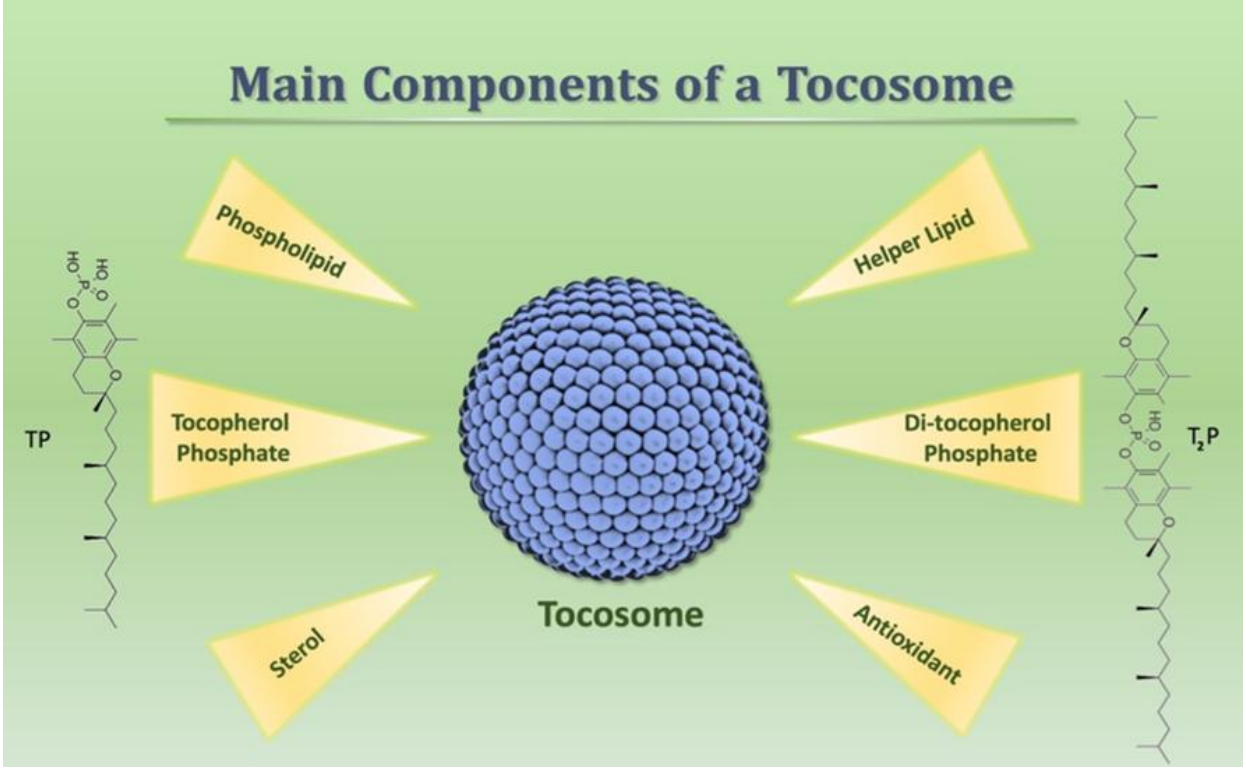


Figure 2 Tocosome

Advanteges

Intrinsic antioxidant activity due to their vitamin E content, leading to potential anti-inflammatory, cardioprotective, and antitumor benefits beyond the included therapeutic agents [10]

Excellent long-term stability, maintaining integrity and effectiveness for up to two years [11]

Solvent-free, scalable production process using protocols such as the Mozafari method, which avoids harmful organic solvents and harsh chemicals—this makes large-scale and environmentally friendly manufacturing possible [12]
Enhanced bioavailability and targeted, controlled, or sustained release, providing significant therapeutic improvement for complex drug delivery needs [13]

Disadvantages
Limited clinical validation and regulatory approval, as they are a novel technology needing more widespread testing and formal acceptance. [14]
Risks of physical instability, especially if exposed to temperature or pH changes; this can affect performance during extended storage or transport. [15]
Possibility of premature release of the encapsulated compounds if proper stabilization is not maintained during manufacturing or preservation [16]
Technical challenges in manufacturing, especially for achieving reliably high stability without employing solvents or expensive industrial processes [17]

RECENT DRUG USED WITH TOCOSOME

Drug Name	Application Area	Key Notes on Tocosomal Delivery	Reference
5-Fluorouracil	Cancer chemotherapy	Demonstrated narrow size distribution, high encapsulation efficiency, and excellent long-term stability	[The Bioscan, 2025]the bio scan [18]
Sunitinib malate	Metastatic kidney cancer	Encapsulated in temperature-sensitive tocosomal nanocarriers with enhanced stability and industrial production potential	[PMC, 2024]pmc.ncbi.nlm.nih [19]
Sorafenib tosylate	Cancer therapy	Delivers efficiently with temperature-responsive magnetotocosome for magnetic targeting	[ScienceDirect, 2023]sciencedirect [20]
Paclitaxel (as TPGS carrier)	Ovarian cancer	Modified tocopherol-based carriers improving efficacy and reducing drug resistance in tumor cells	[PMC, 2024]pmc.ncbi.nlm.nih [21]

HYDROGEL
Hydrogels are crosslinked polymer chains with three-dimensional (3D) network structures, which can absorb relatively large amounts of fluid. Because of the high-water content, soft structure, and porosity of hydrogels, they closely resemble living tissues. Research in recent years shows that hydrogels have been applied in various fields, such as agriculture, biomaterials, the food industry, drug delivery, tissue engineering, and regenerative medicine. Hydrogels comprise a three-

dimensional (3D) network which can absorb a large amount of water and swell in the water due to their hydrophilic groups, such as -NH_2, -COOH, -OH, -$CONH_2$, -CONH, and -SO_3H. [22]
The ability of hydrogels to absorb water arises from hydrophilic functional groups attached to the polymeric backbone, while their resistance to dissolution arises from cross-links between network chains. Many materials, both naturally occurring and synthetic. hydrogels have been defined as two- or multi-component systems consisting of a three-dimensional network of polymer chains and water that fills the space between macromolecules1. [23]

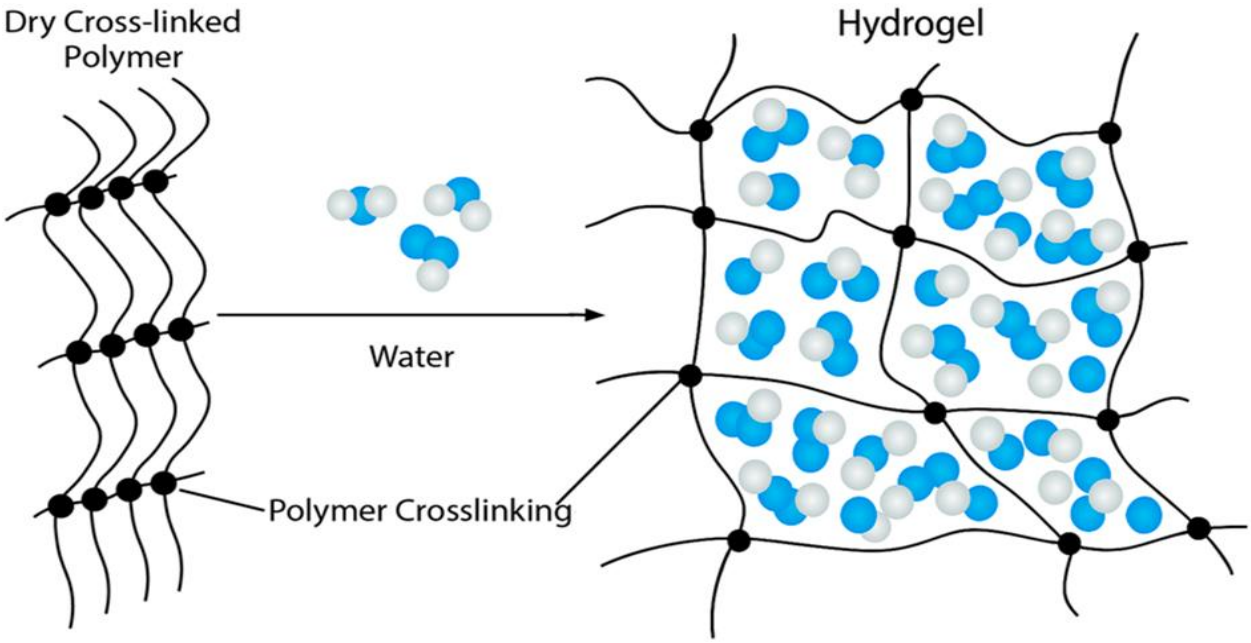


Figure 3 Hydrogel

Advantages
Biocompatibility, biodegradability, and nontoxicity Hydrogels are generally safe for biomedical use, making them ideal for drug delivery, tissue engineering, and other clinical applications [24]
Controlled and sustained drug release: Hydrogels are capable of holding and gradually releasing drugs, reducing dosing frequency and providing prolonged therapeutic effects [25]
Mimic natural tissue environment: Their porous, soft, and hydrated structure closely resembles living tissues, promoting cell growth, adhesion, and proliferation [26]

Disadvantages
Some hydrogels, especially synthetic ones, may retain toxic ingredients from the polymerization or crosslinking process (e.g., residual monomers, initiators, or photo-initiators), raising safety concerns for in vivo applications [27]
Hydrogel scaffold physical properties (e.g., stiffness, pore size, viscoelasticity) need to be meticulously tuned for each application, as improper design can disrupt cell division, differentiation, and general bio functionality [28]

he transitions from bench-scale hydrogel preparation to mass production faces hurdles in reproducibility, scalability, and regulatory approval. [29]

RECENT DRUG USED IN HYDROGEL PREPARATION

Drug/Agent	Therapeutic Area	Hydrogel Type / Format	Key Purpose / Benefit	Reference
Doxorubicin	Cancer (local therapy)	Injectable hydrogel	Sustained and localized chemotherapy	[PubMed, 2025]pubmed.ncbi.nlm.nih [30]
Insulin	Diabetes	Stimuli-responsive hydrogel	Responds to glucose for controlled insulin release	[IJPS, 2025]ijpsjournal [31]
Growth factors (e.g., VEGF, bFGF)	Tissue regeneration	Thermosensitive hydrogel	Promotes wound healing and tissue repair	[ScienceDirect, 2024]sciencedirect [32]
Monoclonal antibodies (e.g., anti-TNF)	Inflammatory diseases	Nanocomposite hydrogel	Enhances local bioavailability for IBD therapy	[RSC, 2024]pubs.rsc [33]
Cisplatin	Cancer	Hybrid hydrogel-scaffold	Reduces systemic toxicity, improves tumor targeting	[ScienceDirect, 2025]sciencedirect [34]

MICRONIDDLE

Microneedle, as a novel drug delivery system consisting of an array of microscale needles, has attracted widespread attention due to its non-invasiveness, simple operation, topical and controllable drug delivery, and diverse cargo loading capacity. Although microneedles are initially designed to penetrate the stratum corneum of the skin for transdermal drug delivery. Microneedles have unique advantages in the wound healing and tissue regeneration. The microscale needle tips can easily pass through the physical barriers at wound sites, like clots, scars, and exudates, and sustainably release drugs. [35] Microneedles typically measure 0.1–1 mm in length. [36] The application of microneedle patches to the skin produces micro sized pathways for transporting molecules, including biomedical antigens and cells. There have been many studies of microneedles for applications such as drawing blood and interstitial fluid (ISF) or delivering low and high molecular weight biotherapeutics, drugs, and vaccines through the skin. [37]

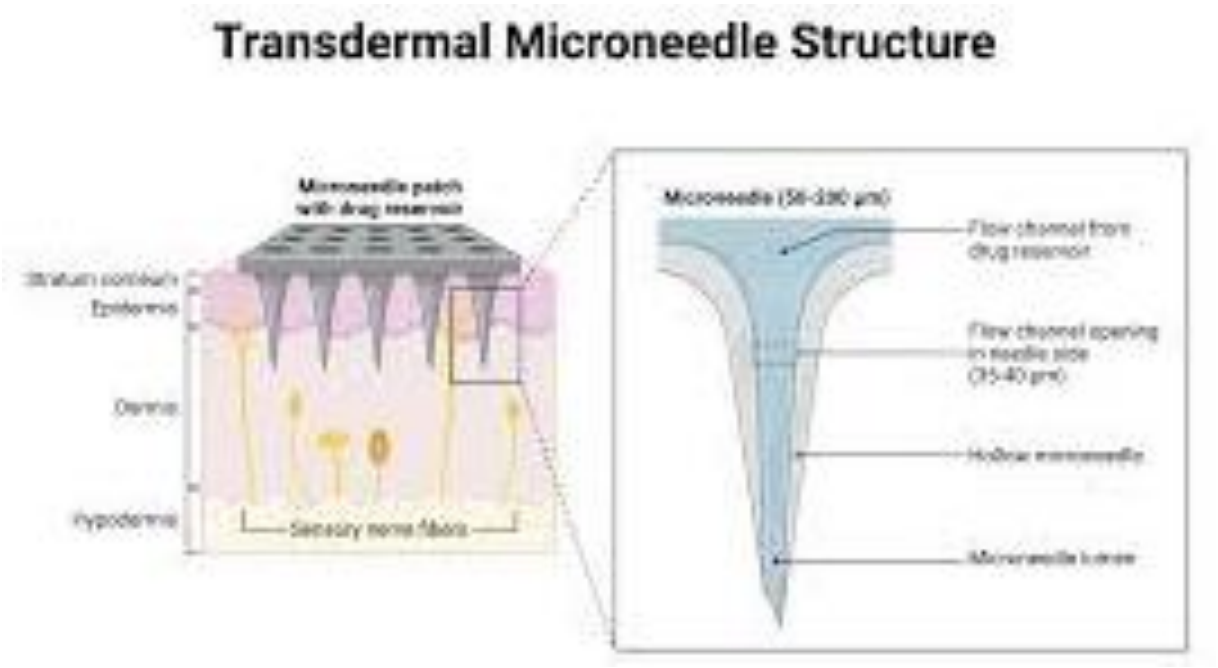


Figure 4 microneedle

Advantages

Enables painless and minimally invasive drug or vaccine administration, significantly improving patient comfort and compliance.

Delivers drugs directly across the stratum corneum, facilitating rapid systemic absorption and bypassing the gastrointestinal tract and first-pass metabolism

Reduces the risk of needlestick injuries and associated biohazardous waste

Allows for self-administration and reduces the need for trained healthcare professionals [38]

Disadvantages

Drug loading capacity is limited due to small size, making high-dose delivery challenging. [39]

Potential for local skin irritation, temporary inflammation, or allergy at the application site

Requires sophisticated fabrication technology and quality control for reproducibility and safety. [40]

Mechanical fragility: microneedles may break and leave fragments in the skin, especially if not properly designed or applied [41]

Drugs Delivered by Microneedles [42]

Drug/Category	Clinical Indication	Therapeutic Uses
Parathyroid hormone	Osteoporosis	Management of osteoporosis, improved bone mineral density, repair of bone tissue, possible tendon healing

Drug/Category	Clinical Indication	Therapeutic Uses
Lidocaine	Local anesthesia	Rapid induction of anesthesia for minor skin procedures, pain relief
Piroxicam	Anti-inflammatory	Localized anti-inflammatory action, pain relief in musculoskeletal disorders
Desmopressin	Diabetes insipidus, Hemophilia	Management of central diabetes insipidus and bleeding in hemophilia by non-invasive administration

NANOBOT

Nanotechnology has greatly influenced modern healthcare and medicine, especially through the innovation of nanobots, which have transformed pharmaceutical drug delivery and cancer treatment. Nanobots are microscopic robotic systems capable of navigating through the human body to specifically target cancerous cells and deliver therapeutic agents with remarkable precision. This targeted approach helps protect healthy tissues, minimizes adverse side effects, and improves the overall effectiveness of treatment. In addition, nanobots hold promise for real-time monitoring**,** early disease detection, and controlled drug release, making them highly valuable in cancer therapy. This review focuses on the design, working principles, and recent advancements of nanobot technology, as well as its potential future applications in medicine. [43]

Advantages

DEEP TISSUE TARGETING:

Nanobots can move into deep tissues for treatment or surgery.

They help reduce surgical risks and speed up recovery.

Sensors in nanobots detect biological signals and adjust drug delivery in real time. [44]

EARLY DISEASE DETECTION:

Nanobots with biosensors can identify DNA mutations and biomarkers.

They enable real-time and accurate disease diagnosis. [45]

CONTINUOUS MONITORING:

Nanobots can monitor the body continuously and collect data.

This helps in creating personalized and effective therapies. [46]

Disadvantages

BIOCOMPATIBILITY AND TOXICITY CONCERNS:

Some materials used in nanobot construction, such as metals and carbon-based nanostructures, can trigger immune responses or cause cytotoxicity and environmental risks. Ensuring full biocompatibility remains a major challenge. [47]

REGULATORY AND SAFETY HURDLES:
Extensive preclinical and clinical studies are required to confirm the long-term safety and effectiveness of nanobots. The lack of clear regulatory guidelines delays their approval for clinical use. [48]

PRODUCTION AND SCALABILITY ISSUES:
Designing and manufacturing nanobots with precision and consistency on a large scale is technologically demanding and expensive, limiting commercial feasibility. [49]

IN VIVO STABILITY AND CLEARANCE:
Nanobots may lose functionality inside the body due to enzymatic degradation, immune clearance, or difficulty in reaching specific tissues or cells. [50]

*E*xamples of medical nanobots. [51] [52]

Nanobot Type	Drug Delivered	Targeting Strategy	Site of Action
\RVG-MSP-FLAG Nanorobot	GAPDH siRNA	Surface marker targeting, IV delivery	Neural tissue (Neuro-2A)
G4-DOX-PEG-Tf-TAM Nanobot	Doxorubicin (DOX)	BBB transporter, pH-sensitive release	Glioma (brain tumor)
TAT-Au NP Nanobot	Doxorubicin (DOX)	BBB-crossing, nanocarrier technology	Brain tumor (U87 cells)
Microbivore Nanobot	Bacterial debris	Synthetic phagocytosis	Bloodstream
Respirocyte Nanobot	Oxygen	Artificial red blood cell replacement	Systemic circulation
Self-propelling Magnetic Nanobot	Anticancer drugs	Magnetic field-guided	Tumor

III. NOVEL DRUG DELIVERY SYSTEMS (NDDS) USED FOR VARIOUS DISEASES

Introduction

Novel Drug Delivery Systems (NDDS) have significantly advanced modern therapeutics by enhancing drug specificity, minimizing systemic toxicity, and improving patient adherence [53–55]. These systems have demonstrated substantial applications across multiple medical fields, including oncology, infectious diseases, cardiovascular disorders, diabetes, neurological and ophthalmic conditions, as well as inflammatory and autoimmune diseases [54,56,58]. This review

summarizes recent progress (2020–2025) in NDDS applications, focusing on therapeutic outcomes and translational challenges without delving into individual system classifications [57–59]. Conventional drug delivery approaches often encounter limitations such as poor bioavailability, off-target distribution, and dose-related toxicity [53,58,60]. NDDS address these shortcomings by modulating pharmacokinetic and pharmacodynamic profiles, ensuring optimal drug concentration at the site of action [55,59]. Over the past five years, the global NDDS market has experienced rapid expansion due to innovations in mRNA vaccines, long-acting injectables, and targeted nanocarrier formulations [56,57,61]. Consequently, NDDS have become integral to the management of chronic, infectious, and degenerative diseases [54,58,62].

NDDS Applications in Oncology

Cancer therapy remains one of the most significant beneficiaries of NDDS technology. Controlled-release formulations and tumor-targeted delivery have improved therapeutic indices of chemotherapeutics. Clinical applications such as targeted doxorubicin formulations and mRNA-based immunotherapies have demonstrated prolonged survival with reduced adverse effects [63–67]. Furthermore, personalized NDDS tailored to tumor microenvironments allow precision delivery of immunomodulators, siRNA, and checkpoint inhibitors [68–70]. Integration with imaging (theranostics) enhances tumor localization and monitoring.

NDDS in Infectious Diseases

NDDS play a vital role in combating infectious diseases through improved delivery of antimicrobials, vaccines, and antiviral agents. During the COVID-19 pandemic, mRNA vaccine platforms highlighted NDDS as a cornerstone of modern vaccinology [71–74]. Similar approaches are now being applied to tuberculosis, HIV, malaria, and emerging viral infections [75–77]. Sustained drug release and targeted pathogen interaction reduce resistance and improve therapeutic adherence. Formulations enabling pulmonary or mucosal delivery have further enhanced efficacy against respiratory infections [78–79].

NDDS for Cardiovascular Disorders

Cardiovascular diseases benefit from localized and sustained delivery strategies that improve vascular repair and prevent restenosis. Controlled-release drug systems have revolutionized stent technology and post-angioplasty care [80–81]. Injectable NDDS targeting ischemic tissues facilitate site-specific drug deposition, minimizing systemic exposure. Emerging studies demonstrate improved outcomes using biologics and growth factors administered via NDDS to promote cardiac regeneration and neovascularization [82–84].

NDDS in Diabetes and Endocrine Disorders

In diabetes management, NDDS ensure continuous or stimuli-responsive insulin release and better glycemic control. Long-acting injectables, smart-release systems, and oral insulin NDDS have shown improved patient adherence and glycemic stability [85–86]. Additionally, NDDS for GLP-

1 analogues and DPP-4 inhibitors enhance therapeutic longevity and bioavailability. Endocrine disorder treatments increasingly rely on hormone delivery systems designed for sustained pharmacologic action [87–88].

NDDS in Neurological and Psychiatric Disorders

One of the major challenges in neuropharmacology is overcoming the blood–brain barrier (BBB). NDDS have provided novel routes for brain targeting, including systemic and intranasal administration of neuroactive drugs [89–90]. Enhanced delivery of antiepileptic, antidepressant, and neuroprotective agents has been demonstrated in preclinical and clinical settings [91–92]. Controlled and targeted NDDS reduce dose frequency and side effects in Parkinson's and Alzheimer's management [93].

NDDS in Ophthalmic and Otologic Disorders

Ocular and otologic treatments face significant delivery challenges due to biological barriers. NDDS achieve sustained intraocular or intratympanic drug release, improving therapy for glaucoma, age-related macular degeneration, and chronic otitis [94–96]. Long-acting injectable NDDS reduce dosing frequency and enhance patient compliance. Combination therapies using NDDS for anti-VEGF agents show promising clinical results [97].

NDDS for Inflammatory and Autoimmune Diseases

Inflammatory diseases such as rheumatoid arthritis, inflammatory bowel disease, and psoriasis have seen major improvements with NDDS-mediated targeted therapy [98–100]. By focusing on inflamed tissues, NDDS reduce systemic corticosteroid exposure and side effects. Controlled delivery of anti-TNF agents, methotrexate, and biologics has improved disease remission rates [101]

IV. CONCLUSION

Novel drug delivery systems (NDDS) have revolutionized modern therapeutics by providing enhanced specificity, controlled release, and improved safety profiles compared to conventional methods. Progress in nanotechnology, hydrogels, microneedles, liposomes, tocosomes, and nanobots enables the targeting of diseased tissues, optimizes drug efficacy, and reduces toxicity for diverse clinical indications. Translational advancements in NDDS have demonstrated improved outcomes in areas like cancer treatment, infectious and cardiovascular diseases, diabetes, neuronal disorders, and regenerative medicine. However, challenges remain in biocompatibility, production scalability, long-term safety, and regulatory approval. Future research should focus on overcoming these limitations and validating NDDS across broader clinical trials to ensure their widespread adoption and patient benefit. NDDS exemplify a key direction for pharmaceutical innovation, holding the promise to transform therapeutic strategies for multiple diseases in the coming years

REFRENCES

[1] Chen, Q., Yang, Z., Liu, H., et al. (2024). Novel drug delivery systems: An important direction for drug innovation research and development. *Pharmaceutics*, 16*(5), 674. https://doi.org/10.3390/pharmaceutics16050674

[2] Lv, Y., Li, W., Liao, W., et al. (2024). Nano-drug delivery systems based on natural products. International *Journal of Nanomedicine*, *19*, 541–569. https://doi.org/10.2147/IJN.S443692

[3] Singh, P., & Bhatia, T. (2025). Conventional versus nanotechnology for drug delivery system – A review. *International Journal of Recent Scientific Research*, *16*(3), 0035C

[4] Bose, P., & Craig, M. (2024, March 12). Nanomedicine: Advantages and disadvantages. *AZoNano*. https://www.azonano.com/article.aspx?ArticleID=6711

[5] Iqbal, H. M. N., Rodriguez, A. M. V., Khandia, R., Munjal, A., & Dhama, K. (2017). Recent trends in nanotechnology-based drugs and formulations for targeted therapeutic delivery. *Recent Patents on Inflammation & Allergy Drug Discovery*, *10*(2), 86–93. https://doi.org/10.2174/1872213X10666161213162823

[6] hen Q, Yang Z, Liu H, et al. Novel Drug Delivery Systems: An Important Direction for Drug Innovation Research and Development. *Pharmaceutics*. 2024;16(5):674. Published 2024 May 16. doi:10.3390/pharmaceutics16050674

[7] Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: structure, composition, types, and clinical applications. *Heliyon*. 2022;8(5): e09394. Published 2022 May 13. doi: 10.1016/j.heliyon. 2022.e09394

[8] Divyasree R, Divya K, Aarti S, Bhavani K, Vamsidhar M, Bhanja SB, Sudhakar M, Panigrahi BB. A comprehensive review on liposomes: a novel drug delivery system

[9] Atrooz, O., Kerdari, E., Mozafari, M. R., Reihani, N., Asadi, A., Torkaman, S., Alavi, M., & Taghavi, E. (2024). A comparative review of tocosomes, liposomes, and nanoliposomes as potent and novel nanonutraceutical delivery systems for health and biomedical applications. *Biomedicines*, *12*(9), 2002. https://doi.org/10.3390/biomedicines12092002

[10] Zarrabi A, Alipoor Amro Abadi M, Khorasani S, et al. Nanoliposomes and Tocosomes as Multifunctional Nanocarriers for the Encapsulation of Nutraceutical and Dietary Molecules. *Molecules*. 2020;25(3):638. Published 2020 Feb 1. doi:10.3390/molecules25030638

[11] Sivaram R, H. Gayathri, N. Damodaran. Tocosome: A Cutting-Edge Drug Delivery Platform Combining Phospholipids and Tocopheryl Phosphates. The Bioscan [Internet]. 2025 Jun. 27 [cited 2025 Sep. 23];20(Supplement 2):871-7. Available from: https://thebioscan.com/index.php/pub/article/view/3678

[12] Mozafari MR, Javanmard R, Raji M. Tocosome: Novel drug delivery system containing phospholipids and tocopheryl phosphates. Int J Pharm. 2017;528(1-2):381-2. doi: 10.1016/j.ijpharm.2017.06.037

[13] Palma AS, Casadei BR, Lotierzo MC, de Castro RD, Barbosa LRS. A short review on the applicability and use of cubosomes as nanocarriers. *Biophys Rev*. 2023;15(4):553-567. Published 2023 Aug 7. doi:10.1007/s12551-023-01089-y

[14] Atrooz, O., Kerdari, E., Mozafari, M. R., Reihani, N., Asadi, A., Torkaman, S., Alavi, M., & Taghavi, E. (2024). A Comparative Review of Tocosomes, Liposomes, and Nanoliposomes as Potent and Novel Nanonutraceutical Delivery Systems for Health and Biomedical Applications. *Biomedicines, 12*(9), 2002. https://doi.org/10.3390/biomedicines12092002

[15] Mozafari MR, Javanmard R, Raji M. Tocosome: Novel drug delivery system containing phospholipids and tocopheryl phosphates. Int J Pharm. 2017;528(1-2):381-2. doi: 10.1016/j.ijpharm.2017.06.037

[16] Zarrabi A, Alipoor Amro Abadi M, Khorasani S, et al. Nanoliposomes and Tocosomes as Multifunctional Nanocarriers for the Encapsulation of Nutraceutical and Dietary Molecules. *Molecules*. 2020;25(3):638. Published 2020 Feb 1. doi:10.3390/molecules25030638

[17] Sivaram R, H. Gayathri, & N. Damodaran. (2025). Tocosome: A Cutting-Edge Drug Delivery Platform Combining Phospholipids and Tocopheryl Phosphates. *The Bioscan, 20*(Supplement 2), 871–877. https://doi.org/10.63001/tbs.2025.v20.i02.S2.pp871-877

[18] Sivaram R, H. Gayathri, N. Damodaran. Tocosome: A Cutting-Edge Drug Delivery Platform Combining Phospholipids and Tocopheryl Phosphates. The Bioscan [Internet]. 2025 Jun. 27 [cited 2025 Oct. 8];20(Supplement 2):871-7. Available from: https://thebioscan.com/index.php/pub/article/view/3678

[19] Chen, Q., Yang, Z., Liu, H., Man, J., Oladejo, A. O., Ibrahim, S., Wang, S., & Hao, B. (2024). Novel Drug Delivery Systems: An Important Direction for Drug Innovation Research and Development. *Pharmaceutics*, *16*(5), 674. https://doi.org/10.3390/pharmaceutics16050674

[20] Razmimanesh F, Sodeifian G. Evaluation of a temperature-responsive magnetotocosome as a magnetic targeting drug delivery system for sorafenib tosylate anticancer drug. Heliyon. 2023;9(11): e21794. doi: 10.1016/j.heliyon. 2023.e21794

[21] Chen, Q., Yang, Z., Liu, H., Man, J., Oladejo, A. O., Ibrahim, S., Wang, S., & Hao, B. (2024). Novel Drug Delivery Systems: An Important Direction for Drug Innovation Research and Development. *Pharmaceutics*, *16*(5), 674. https://doi.org/10.3390/pharmaceutics16050674

[22] Ho TC, Chang CC, Chan HP, et al. Hydrogels: Properties and Applications in Biomedicine. *Molecules*. 2022;27(9):2902. Published 2022 May 2. doi:10.3390/molecules27092902

[23] Ahmed EM. Hydrogel: Preparation, characterization, and applications: A review. J Adv Res. 2015;6(2):105-21. doi: 10.1016/j.jare.2013.07.006.9]

[24] Raeisi A, Farjadian F. Commercial hydrogel product for drug delivery based on route of administration. *Frontiers in Chemistry*. 2024; 12:1336717. doi:10.3389/fchem.2024.1336717]

[25] Vigata M, Meinert C, Hutmacher DW, Bock N. Hydrogels as Drug Delivery Systems: A Review of Current Characterization and Evaluation Techniques. *Pharmaceutics*. 2020;12(12):1188. Published 2020 Dec 7. doi:10.3390/pharmaceutics12121188]

[26] Hossein Chamkouri, Mahyodin Chamkouri. A Review of Hydrogels, Their Properties and Applications in Medicine. Am J Biomed Sci & Res. 2021 - 11(6). AJBSR.MS.ID.001682. DOI:10.34297/AJBSR.2021.11.001682.

[27] El-Sherbiny IM, Yacoub MH. Hydrogel scaffolds for tissue engineering: Progress and challenges. *Glob Cardiol Sci Pract*. 2013;2013(3):316-342. Published 2013 Nov 1. doi:10.5339/gcsp.2013.38

[28] Cao, H., Duan, L., Zhang, Y. *et al.* Current hydrogel advances in physicochemical and biological response-driven biomedical application diversity. *Sig Transduct Target Ther* 6, 426 (2021). https://doi.org/10.1038/s41392-021-00830-x

[29] Chauhan N, Saxena K, Jain U. Hydrogel based materials: A progressive approach towards advancement in biomedical applications. Mater Today Commun. 2022; 33:104369. doi: 10.1016/j.mtcomm.2022.104369

[30] Dinh, L., Hwang, S. J., & Yan, B. (2025). Hydrogel Conjugation: Engineering of Hydrogels for Drug Delivery. *Pharmaceutics*, *17*(7), 897. https://doi.org/10.3390/pharmaceutics17070897

[31] Muralidhar S, Ramya K, Rajeev Sri Sasikar G, Suvarna Ratnam G, Poornima G, Ramya J, Sai Ananth Varma J. Hydrogel-based drug delivery: From traditional formulations to advanced applications. Published 2025 Apr 30. doi:10.5281/zenodo.15309586

[32] Lin X, Zhang X, Wang Y, Chen W, Zhu Z, Wang S. Hydrogels and hydrogel-based drug delivery systems for promoting refractory wound healing: Applications and prospects. Int J Biol Macromol. 2025; 285:138098. doi: 10.1016/j.ijbiomac.2024.138098.

[33] Liu Y, Huang J, Li S, Li Z, Chen C, Qu G, Chen K, Teng Y, Ma R, Wu X, Ren J. Advancements in hydrogel-based drug delivery systems for the treatment of inflammatory bowel disease: a review. *Biomater Sci*. 2024; 12:837–862. doi:10.1039/D3BM01645E

[34] Guo A, Cao Q, Fang H, Tian H. Recent advances and challenges of injectable hydrogels in drug delivery. J Control Release. 2025; 385:114021. doi: 10.1016/j.jconrel.2025.114021.

[35] Lyu S, Dong Z, Xu X, Bei HP, Yuen HY, Cheung CWJ, Wong MS, He Y, Zhao X. Going below and beyond the surface: Microneedle structure, materials, drugs, fabrication, and applications for wound healing and tissue regeneration. Bioact Mater. 2023; 27:303-326. doi: 10.1016/j.bioactmat.2023.04.003Aldawood

[36] FK, Andar A, Desai S. a Comprehensive Review of Microneedles: Types, Materials, Processes, Characterizations and Applications. *Polymers (Basel)*. 2021;13(16):2815. Published 2021 Aug 22. doi:10.3390/polym13162815

[37] An overview of microneedle applications, materials, and fabrication methods Zahra Faraji Rad, Philip D. Prewett and Graham J. Davies *Beilstein J. Nanotechnol.* 2021, *12*, 1034–1046.https://doi.org/10.3762/bjnano.12.77

[38] Jung, J. H., & Jin, S. G. (2021). Microneedle for transdermal drug delivery: current trends and fabrication. *Journal of pharmaceutical investigation*, *51*(5), 503–517. https://doi.org/10.1007/s40005-021-00512-4

[39] Avcil, M., & Çelik, A. (2021). Microneedles in Drug Delivery: Progress and Challenges. *Micromachines*, *12*(11), 1321. https://doi.org/10.3390/mi12111321

[40] Aldawood, F. K., Andar, A., & Desai, S. (2021). A Comprehensive Review of Microneedles: Types, Materials, Processes, Characterizations and Applications. *Polymers*, *13*(16), 2815. https://doi.org/10.3390/polym13162815

[41] Hamdan I (2024) Microneedle and drug delivery across the skin: An overview. Pharmacia 71: 1–12. https://doi.org/10.3897/ pharmacia.71. e112503

[42] Prausnitz MR, Langer R. Microneedles: A new paradigm in transdermal delivery of therapeutic agents. *Nature Biotechnology*. 2004;22(11):1261–1268. doi:10.1038/nbt1004-1261

[43] Shrivastava P, Uikey AR, Sakharwade A, Kumar A, Meher A, Tiwari SP. Nanobots in Pharmacy: A Futuristic Approach to Drug Delivery and Therapeutics. J Neonatal Surg [Internet]. 2025May24 [cited 2025Oct.30];14(27S):461-70. Available from: https://www.jneonatalsurg.com/index.php/jns/article/view/6429

[44] Kong, X., Gao, P., Wang, J., Fang, Y., & Hwang, K. C. (2023). *Advances of medical* nanorobots *for future cancer treatments. Journal of Hematology & Oncology*, 16(1), 74. https://doi.org/10.1186/s13045-023-01463-z

[45] Himabindu, A. V. S., Krupamai, G., Pravallika, K., Saranya, U., Kavya, P., Devika, S., & Padmalatha, K. (2025). *Nanorobotics in Targeted Drug Delivery System. Asian Journal of Pharmacy and Technology*, 15(1), 95–100. https://doi.org/10.52711/2231-5713.2025.00016

[46] Shrivastava, P., Uikey, A. R., Sakharwade, A., Kumar, A., Meher, A., & Tiwari, S. P. (2025). *Nanobots in Pharmacy: A Futuristic Approach to Drug Delivery and Therapeutics. Journal of Neonatal Surgery*, 14(27s), 461–470

[47] Jeevanandam, J., Barhoum, A., Chan, Y. S., Dufresne, A., & Danquah, M. K. (2018). Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. *Beilstein Journal of Nanotechnology*, 9, 1050–1074

[48] Saini, R. (2017). Nanorobots: Future of healthcare system. *International Journal of Current Research*, 9(12), 63161–63164

[49] Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., Rodriguez-Torres, M. D. P., Acosta-Torres, L. S., & Shin, H. S. (2018). Nano-based drug delivery systems: recent developments and future prospects. *Journal of Nanobiotechnology*, 16(1), 71

[50] Nelson, B. J., Kaliakatsos, I. K., & Abbott, J. J. (2010). Microrobots for minimally invasive medicine. *Annual Review of Biomedical Engineering*, 12, 55–85.

[51] Xu M, Qin Z, Chen Z, Wang S, Peng L, Li X, Yuan Z. Nanorobots mediated drug delivery for brain cancer active targeting and controllable therapeutics. Discov Nano. 2024 Nov 14;19(1):183. doi: 10.1186/s11671-024-04131-4. PMCID: PMC11564721

[52] Nanobots for Medicinal Applications. Austin Journal of Nanomedicine & Nanotechnology. 2023;11(5):1067. Available from: https://austinpublishinggroup.com/nanomedicine-nanotechnology/fulltext/ajnn-v11-id1067.php

[53] Patra JK, Das G, Fraceto LF, Campos EVR, Rodriguez-Torres MDP, Acosta-Torres LS, et al. *Nano-based drug delivery systems: recent developments and future prospects.* J Nanobiotechnology. 2018;16(1):71.

[54] Zhou Y, Gao P, Wang J, Fang Y, Hwang KC. *Advances of medical nanorobots for future* cancer *treatments.* Adv Drug Deliv Rev. 2025; 215:115622.

[55] Wang H, Liu Y, Zhang J, Li X, Chen L. *Recent advances in targeted nanocarrier-based* drug *delivery for precision medicine.* Nat Commun. 2025; 16:2281.

[56] Sahin U, Karikó K, Türeci Ö. *mRNA-based therapeutics—developing a new class of drugs.* Nat Rev Drug Discov. 2023;22(8):595–613.

[57] Pardi N, Hogan MJ, Porter FW, Weissman D. *mRNA vaccines—a new era in vaccinology.* Nature. 2021; 597:410–416.

[58] Gupta A, Pandey AK, Thomas G, Sethi S, Shukla S, Singh N. *Advances in nanotechnology for targeted drug delivery systems.* Drug Deliv Transl Res. 2022;12(8):1763–1778.

[59] Li M, Zhao X, Zhang X, Yang Y, Wang J. *Recent progress in controlled and targeted drug* delivery *using nanocarriers.* J Control Release. 2024; 386:115092.

[60] Al-Harthi SH, Mohaisen KO, Al-Abbasi FA, Al-Hosaini K, Alshehri S. *Recent advances in nanocarriers for drug delivery and controlled release.* Expert Opin Drug Deliv. 2024;21(1):37–50.

[61] Chahal JS, Khan OF, Cooper CL, McPartlan JS, Tsosie JK, Tilley LD, et al. *Nanoparticle* engineering *for vaccine delivery and drug transport.* Adv Sci. 2024;11(14):2400123.

[62] Barhate S, Kaur R, Singh D, Mehta T. *Recent advances in nanopharmaceutical* formulations *for improved bioavailability.* Front Pharmacol. 2025; 16:128222.

[63] Chen X, et al. *Recent developments in nanoparticle-mediated drug delivery.* Int J Pharm. 2023; 629:122420.

[64] Li M, et al. *Novel approaches in controlled drug release.* J Control Release. 2024; 386:115092.

[65] Rajput S, et al. *A review of nanocarriers for drug delivery.* Pharmaceutics. 2023;15(4):982.

[66] Gupta A, et al. *Advances in nanotechnology for drug delivery.* Drug Deliv Transl Res. 2022;12(8):1763–1778.

[67] Wang H, et al. *Next-generation nanomaterials in drug delivery.* Nat Commun. 2025; 16:2281.

[68] Al-Harthi SH, et al. *Targeted drug delivery using nanocarriers.* Expert Opin Drug Deliv. 2024;21(1):37–50.

[69] Jin L, et al. *Nanoparticle-based drug delivery: mechanisms and applications.* Mol Pharm. 2023;20(6):2289–2302.

[70] Pardi N, et al. *mRNA vaccines—a new era in vaccinology.* Nature. 2021; 597:410–416.

[71] Sahin U, et al. *mRNA-based therapeutics and vaccines.* Nat Rev Drug Discov. 2023; 22:595–613.
[72] Chahal JS, et al. *Nanoparticle engineering for drug delivery.* Adv Sci. 2024;11(14):2400123.
[73] Zhang Z, et al. *Advances in nanovaccine technology.* Vaccine. 2024;42(5):1260–1275.
[74] Singh P, et al. *Emerging trends in nanomedicine.* Pharm Res. 2023; 40:1876–1890.
[75] Hoang LT, et al. *Nanobiotechnology in drug delivery.* J Nanobiotechnol. 2024; 22:100.
[76] Kumar R, et al. *antimicrobial nanomaterials.* Int J Antimicrob Agents. 2022; 59:106479.
[77] Barhate S, et al. *Recent advances in nanopharmaceuticals.* Front Pharmacol. 2025; 16:128222.
[78] Tiwari A, et al. *Novel nanocarriers for drug delivery.* J Drug Deliv Sci Technol. 2024; 87:104578.
[79] Bose D, et al. *Biopolymer-based nanocarriers.* Biomater Sci. 2024;12(3):894–908.
[80] Mendez R, et al. *Nanotechnology for cardiovascular therapy.* Cardiovasc Drug Ther. 2023;37(2):125–140.
[81] Zhu Y, et al. *Nanocarriers for gene therapy.* Front Bioeng Biotechnol. 2024; 12:144021.
[82] Kim JW, et al. *Nanotechnology in cancer therapy.* ACS Nano. 2023;17(9):8971–8988.
[83] Akhtar MS, et al. *Recent advances in nanomedicine.* Biomed Pharmacother. 2024; 176:114592.
[84] Chou DH, et al. *Nanotechnology in diabetes management.* Diabetes Care. 2025;48(1):45–57.
[85] Karthik S, et al. *Targeted nanodelivery systems.* J Control Release. 2023; 385:115016.
[86] Wu L, et al. *Nanoparticles in drug delivery: recent advances.* Eur J Pharm Biopharm. 2024; 198:17–28.
[87] Saha S, et al. *Nanocarriers for drug targeting.* Mol Pharm. 2022;19(11):3910–3925.
[88] Patel HR, et al. *Nanotechnology in neuropharmacology.* Brain Res Bull. 2023; 205:181–193.
[89] Zhang L, et al. *Recent developments in nanomedicine.* Adv Drug Deliv Rev. 2025; 218:115633.
[90] Chen J, et al. *Advances in nanocarrier-based drug delivery.* CNS Drugs. 2023;37(8):671–684.
[91] Ghosh A, et al. *Nanotechnology for neurotherapeutics.* Neurotherapeutics. 2024;21(2):299–312.
[92] Iyer R, et al. *Nanodelivery systems in pharmaceutical research.* Pharmaceutics. 2023;15(6):1640.
[93] Dong Y, et al. *Emerging nanotherapeutics.* Drug Discov Today. 2024;29(3):103286.
[94] Lai J, et al. *Ocular nanomedicine.* J Ocul Pharmacol Ther. 2024;40(2):145–159.
[95] Abbas M, et al. *Nanocarriers for drug delivery.* Int J Pharm. 2023; 641:123448.
[96] Singh D, et al. *Advances in nanomedicine.* Pharmaceutics. 2024;16(5):985.
[97] Xu Q, et al. *Nanotechnology in translational medicine.* J Transl Med. 2023;21(1):322.

[98] Rahman MA, et al. *Nanomedicine for immunotherapy.* Front Immunol. 2024; 15:112474.
[99] Nambiar S, et al. *Nanotechnology in drug design.* Drug Des Devel Ther. 2024; 18:423–439.
[100] Chen F, et al. *Recent progress in pharmacology research.* Pharmacol Res. 2025; 198:107018.
[101] Patel R, et al. *Advanced biomaterials for healthcare applications.* Adv Healthc Mater. 2025;14(2):240111.