

REDEFINING DRUG DELIVERY: A REVIEW OF CLINICALLY PROVEN NOVEL DRUG DELIVERY TECHNOLOGIES

Dr. Praveen Kumar R. Biradar^{*1}, Bilquees Mukhtar², Neela Madhav S.³, Ajay Kumar S. N.⁴,
Dr. E. Gopinath⁵

¹Assistant Professor, Department of Pharmacy Practice, Shantha College of Pharmacy, Peresandra, Chikkaballapur-562104, Karnataka, India

²Student, Shantha College of Pharmacy, Peresandra, Chikkaballapur -562104, Karnataka

³Assistant Professor, Department of Pharmacology, Shantha College of Pharmacy, Peresandra, Chikkaballapur-562104, Karnataka, India.

⁴Assistant Professor, Department of Pharmaceutics, Shantha College of Pharmacy, Peresandra, Chikkaballapur-562104, Karnataka, India.

⁵Principal, Department of Pharmaceutics, Shantha College of Pharmacy, Peresandra, Chikkaballapur-562104, Karnataka, India.

Article Received: 22 May 2026 | Article Revised: 12 June 2026 | Article Accepted: 03 July 2026

***Corresponding Author: Dr. Praveen Kumar R. Biradar**

Assistant Professor, Department of Pharmacy Practice, Shantha College of Pharmacy, Peresandra, Chikkaballapur-562104, Karnataka, India

DOI: <https://doi.org/10.5281/zenodo.21371192>

How to cite this Article: Dr. Praveen Kumar R. Biradar, Bilquees Mukhtar, Neela Madhav S., Ajay Kumar S. N., Dr. E. Gopinath (2026) REDEFINING DRUG DELIVERY: A REVIEW OF CLINICALLY PROVEN NOVEL DRUG DELIVERY TECHNOLOGIES. World Journal of Pharmaceutical Science and Research, 5(7), 523-537.



Copyright © 2026 Dr. Praveen Kumar R. Biradar | World Journal of Pharmaceutical Science and Research.

This work is licensed under creative Commons Attribution-NonCommercial 4.0 International license (CC BY-NC 4.0).

ABSTRACT

Novel Drug Delivery Systems (NDDS) have emerged as one of the most important developments in modern pharmaceutical sciences. Traditional dosage forms such as tablets, capsules, and injections often face challenges including poor bioavailability, rapid drug degradation, frequent dosing requirements, and undesirable side effects due to non-specific drug distribution. NDDS has been developed to address these limitations by improving the way drugs are delivered, released, and targeted within the body. Advanced delivery platforms such as liposomes, nanoparticles, transdermal systems, controlled-release formulations, and lipid nanoparticles have significantly enhanced therapeutic outcomes while reducing toxicity and improving patient compliance. This review adopts a case study-based approach to examine the clinical success of five widely recognised NDDS products: liposomal doxorubicin (Doxil®), albumin-bound paclitaxel nanoparticles (Abraxane®), fentanyl transdermal patches, metformin extended-release tablets, and lipid nanoparticle-based mRNA COVID-19 vaccines. Each case study highlights the therapeutic challenge, delivery strategy, clinical benefits, limitations, and future prospects associated with the technology. Furthermore, the review discusses emerging trends including artificial intelligence-assisted formulation development, stimuli-responsive delivery systems, personalised medicine, and theragnostic platforms. Collectively, these advancements demonstrate the transformative role of NDDS in improving patient care and shaping the future of pharmaceutical therapy.

KEYWORDS: Novel Drug Delivery Systems, Liposomes, Nanoparticles, Controlled Release, Transdermal Delivery, Lipid Nanoparticles, Nanomedicine, Targeted Drug Delivery.

1. INTRODUCTION

1.1 Overview of Novel Drug Delivery Systems

The effectiveness of any therapeutic agent depends not only on its pharmacological activity but also on its ability to reach the desired site of action in adequate concentration and for an appropriate duration. Many promising drug molecules fail to achieve their full clinical potential because of poor solubility, low absorption, rapid metabolism, short biological half-life, or extensive distribution to healthy tissues. These limitations often result in reduced therapeutic efficacy and an increased risk of adverse effects. To overcome these challenges, researchers have developed Novel Drug Delivery Systems (NDDS), which are advanced formulation approaches designed to improve the delivery and performance of pharmaceutical agents. Unlike conventional dosage forms, NDDS focuses on controlling the rate, timing, and location of drug release, thereby enhancing treatment effectiveness while minimising toxicity. Over the past few decades, these technologies have become an integral part of pharmaceutical research and development.^[1]

1.2. Importance of NDDS in Modern Therapeutics

The growing importance of NDDS can be attributed to its ability to address major therapeutic challenges that conventional drug delivery systems often fail to solve. Advanced delivery systems can increase drug stability, prolong circulation time, improve tissue targeting, and enhance patient adherence by reducing dosing frequency. These benefits are particularly valuable in the treatment of chronic diseases such as cancer, diabetes, cardiovascular disorders, and infectious diseases.

Targeted drug delivery has become one of the most significant achievements of NDDS. By directing drug molecules toward diseased tissues while limiting exposure to healthy organs, targeted systems can improve therapeutic outcomes and reduce treatment-related toxicity. Such advantages have encouraged the widespread adoption of nanotechnology-based carriers, liposomes, polymeric systems, and controlled-release formulations in clinical practice.^[3]

1.3 Major Types of Novel Drug Delivery Systems

NDDS encompasses a wide range of technologies, each designed to address specific pharmaceutical challenges. Liposomes are phospholipid-based vesicles capable of encapsulating both hydrophilic and lipophilic drugs, thereby enhancing drug stability and reducing toxicity. Nanoparticles, including polymeric and albumin-bound systems, improve drug solubility and facilitate targeted delivery to diseased tissues.

Transdermal drug delivery systems provide a non-invasive route of administration that bypasses first-pass metabolism and offers sustained therapeutic effects. Controlled-release formulations are engineered to release drugs gradually over an extended period, helping to maintain consistent plasma concentrations and improve patient compliance. More recently, lipid nanoparticles have gained global attention due to their successful application in mRNA vaccine delivery, demonstrating the ability of NDDS to support entirely new classes of therapeutics.^[2]

1.4 Clinical Relevance of NDDS

The true value of NDDS lies in its successful translation from laboratory research to clinical application. Several advanced drug delivery technologies have demonstrated substantial improvements in patient outcomes and have become standard treatments in various therapeutic areas. Liposomal formulations have reduced the toxicity associated with anticancer drugs, nanoparticle-based systems have enhanced tumour targeting, transdermal patches have improved pain management, and controlled-release formulations have simplified long-term treatment regimens. The rapid

development and global deployment of lipid nanoparticle-based mRNA vaccines during the COVID-19 pandemic further highlighted the clinical significance of NDDS. These achievements demonstrate that innovative delivery technologies can not only improve existing therapies but also enable entirely new treatment strategies that were previously considered impractical.

1.5 Aim of the Review

This review aims to examine the clinical impact of Novel Drug Delivery Systems through a case study-based approach. Five commercially successful pharmaceutical products have been selected to illustrate how advanced drug delivery technologies have addressed important therapeutic challenges. By analysing their mechanisms, clinical outcomes, limitations, and future developments, this review provides a comprehensive understanding of the role of NDDS in contemporary medicine and its potential future applications.^[5]

2. Case Study

2. 1: Liposomal Drug Delivery: Doxil® (Pegylated Liposomal Doxorubicin)

2.1.1 Disease Context and Therapeutic Challenge: Doxorubicin is one of the most widely prescribed anticancer drugs and is commonly used in the treatment of breast cancer, ovarian cancer, multiple myeloma, and Kaposi's sarcoma. The drug exerts its therapeutic effect by interfering with DNA replication and inhibiting cellular division, ultimately leading to cancer cell death. Despite its proven effectiveness, the clinical use of conventional doxorubicin is limited by its severe dose-dependent cardiotoxicity.^[4]

Repeated administration of free doxorubicin can result in irreversible damage to cardiac muscle tissue. This toxicity is primarily associated with the formation of reactive oxygen species and oxidative stress within cardiomyocytes. As a result, clinicians are often forced to limit the cumulative dose, which may reduce the overall effectiveness of treatment.

Additionally, patients receiving conventional doxorubicin frequently experience adverse effects such as bone marrow suppression, hair loss, nausea, and oral mucositis. These limitations created a strong need for a safer and more targeted delivery system capable of maintaining therapeutic efficacy while reducing systemic toxicity.^[6,7]

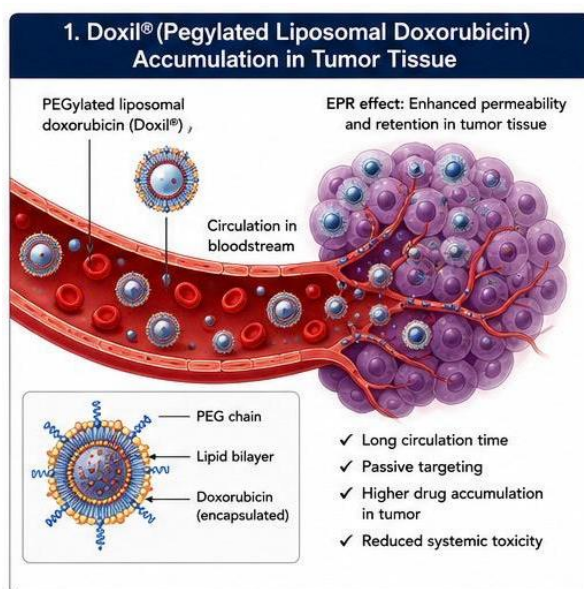


Fig. No. 1: Liposomal Drug Delivery: Doxil® (Pegylated Liposomal Doxorubicin).

2.2 Liposomal Technology and Mechanism of Action: The introduction of Doxil® represented a major milestone in nanomedicine and cancer therapy. Approved by the United States Food and Drug Administration in 1995, Doxil® became the first clinically successful nanotechnology-based anticancer formulation. The drug consists of doxorubicin encapsulated within small PEGylated liposomes composed of phospholipid bilayers. Liposomes act as protective carriers that shield the drug from rapid degradation and minimise direct exposure of healthy tissues to the cytotoxic agent. The addition of polyethylene glycol (PEG) on the liposomal surface creates a protective hydrophilic coating that reduces recognition by the body's immune system. This phenomenon, commonly known as the "stealth effect," allows the liposomes to remain in circulation for a significantly longer period compared to free doxorubicin.^[7]

The prolonged circulation time increases the likelihood of liposome accumulation within tumour tissues through the Enhanced Permeability and Retention (EPR) effect. Tumour blood vessels are often irregular and highly permeable, allowing nanoparticles to pass through and accumulate at the tumour site. Furthermore, poor lymphatic drainage in tumours contributes to prolonged retention of the drug-loaded liposomes. Consequently, higher concentrations of doxorubicin can be delivered directly to cancerous tissues while limiting exposure to healthy organs such as the heart.^[8]

2.3 Clinical Benefits and Therapeutic Outcomes: Several clinical studies have demonstrated the advantages of liposomal doxorubicin over conventional formulations. Patients treated with Doxil® showed comparable or improved anticancer activity while experiencing significantly lower rates of cardiotoxicity. This reduction in cardiac complications has enabled some patients to receive longer treatment courses without exceeding safe cumulative dose limits. Another important benefit of Doxil® is its improved pharmacokinetic profile. The extended circulation time facilitates sustained drug exposure at tumour sites, which can enhance therapeutic effectiveness. In addition, reduced systemic distribution contributes to lower incidences of alopecia and severe bone marrow suppression compared with conventional doxorubicin therapy.

The clinical success of Doxil® has established liposomal drug delivery as an important strategy for improving the therapeutic index of anticancer agents. Its success also encouraged the development of numerous other liposome-based formulations currently used in oncology and other therapeutic areas.^[9]

2.4 Limitations and Future Prospects: Although Doxil® significantly reduces cardiotoxicity, it is not free from adverse effects. One of the most common dose-limiting toxicities associated with the formulation is palmar-plantar erythrodysesthesia, also known as hand-foot syndrome. This condition causes redness, swelling, discomfort, and skin peeling, particularly on the palms and soles. Another challenge is the variability of the EPR effect among patients.

Tumour vascularity differs considerably between individuals and tumour types, meaning that nanoparticle accumulation may not always occur to the same extent. Furthermore, the manufacturing process for liposomal formulations is complex and expensive, which can limit accessibility in certain healthcare settings. Future research is focused on developing actively targeted liposomes capable of recognising specific receptors present on cancer cells. Scientists are also exploring stimuli-responsive liposomes that release their contents in response to pH changes, temperature variations, or enzymatic activity within the tumour microenvironment. These innovations have the potential to further improve targeting accuracy and minimise off-target toxicity.^[10]

3. Case Study 2: Nanoparticle Drug Delivery – Abraxane® (Albumin-Bound Paclitaxel)

3.1 Disease Context and Therapeutic Challenge: Paclitaxel is a highly effective chemotherapeutic agent widely used in the treatment of breast cancer, non-small-cell lung cancer, and pancreatic cancer. The drug acts by stabilising microtubules, thereby preventing normal cell division and promoting cancer cell death. Despite its effectiveness, paclitaxel presents a major formulation challenge because of its extremely poor water solubility. Traditional paclitaxel formulations require the use of Cremophor EL, a solvent system that enables intravenous administration of the drug.

However, Cremophor EL is associated with serious adverse reactions including hypersensitivity, neurotoxicity, and alterations in lipid metabolism. Patients often require corticosteroids and antihistamines before treatment to reduce the risk of severe allergic reactions. These complications can increase treatment burden and negatively affect patient quality of life. The need for a safer formulation capable of eliminating solvent-related toxicity led to the development of nanoparticle-based delivery systems for paclitaxel.^[11]

3.2 Albumin-Bound Nanoparticle Technology: Abraxane® is an innovative nanoparticle formulation in which paclitaxel is bound to human serum albumin to form nanoparticles approximately 130 nanometres in diameter. Albumin is a naturally occurring plasma protein responsible for transporting various hydrophobic molecules throughout the body. By utilising albumin as a carrier, Abraxane® eliminates the need for toxic solvents and takes advantage of natural biological transport mechanisms. Albumin nanoparticles interact with endothelial receptors such as gp60, facilitating transcytosis across blood vessel walls. In addition, many tumours overexpress the protein SPARC (Secreted Protein Acidic and Rich in Cysteine), which has a strong affinity for albumin. This interaction may enhance the accumulation of albumin-bound paclitaxel within tumour tissues. The nanoparticle formulation improves drug solubility, facilitates tumour delivery, and reduces many of the complications associated with conventional paclitaxel formulations.^[12]

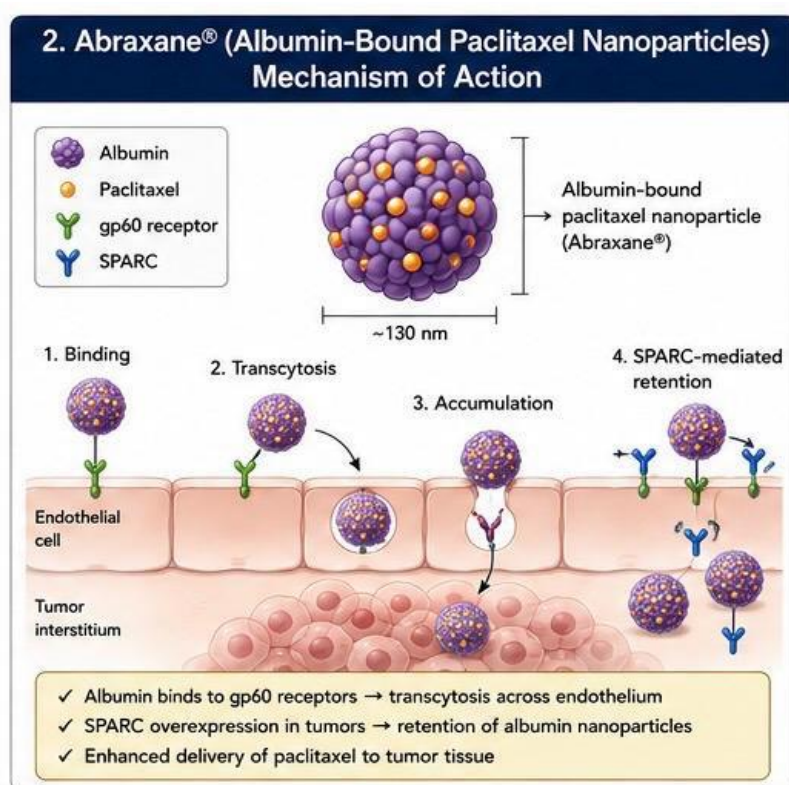


Fig. No. 2: Mechanism of Action of Abraxane.

3.3 Clinical Outcomes and Advantages: Clinical trials have demonstrated several important advantages of Abraxane® over conventional paclitaxel therapy. One of the most significant benefits is the elimination of solvent-related hypersensitivity reactions. As a result, routine premedication with corticosteroids and antihistamines is generally unnecessary, simplifying treatment protocols. Abraxane® has also been associated with improved tumour response rates in several cancers. In metastatic breast cancer, studies reported higher response rates and longer progression-free survival compared with conventional paclitaxel. Similarly, the combination of Abraxane® and gemcitabine significantly improved survival outcomes in patients with metastatic pancreatic cancer. The shorter infusion time and simplified administration procedure further enhance patient convenience and healthcare efficiency. These advantages have contributed to the widespread clinical adoption of albumin-bound nanoparticle technology.^[13]

3.4 Limitations and Future Perspectives: Despite its success, Abraxane® is associated with certain limitations.

Peripheral neuropathy remains a common adverse effect, particularly when higher doses are administered. Although this toxicity is often reversible, it can significantly affect patient quality of life and may necessitate dose modification.

The relatively high cost of nanoparticle-based therapies also presents challenges, particularly in low- and middle-income countries. Furthermore, tumour expression of SPARC varies among patients, which may influence the extent of nanoparticle accumulation and therapeutic response. Future developments are focused on creating multifunctional nanoparticles capable of active targeting, controlled drug release, and simultaneous diagnostic imaging. Researchers are also investigating artificial intelligence-driven approaches to optimise nanoparticle characteristics such as particle size, surface charge, drug loading efficiency, and biodistribution. These advances are expected to improve the precision and effectiveness of nanoparticle-mediated cancer therapy in the coming years.^[14]

4. Case Study 3: Transdermal Drug Delivery – Fentanyl Patch

4.1 Disease Context and Therapeutic Challenge: Chronic pain remains one of the most challenging conditions to manage in modern healthcare, particularly among cancer patients and individuals requiring long-term palliative care.

Fentanyl, a potent synthetic opioid analgesic, is widely used for the management of moderate to severe chronic pain because of its strong analgesic properties and rapid onset of action. However, conventional administration routes such as oral and intravenous delivery are associated with several limitations. When administered orally, fentanyl undergoes extensive first-pass metabolism in the liver, reducing its bioavailability and contributing to variability in therapeutic response among patients. Intravenous administration, although effective, often requires frequent dosing or continuous infusion, which may be inconvenient and uncomfortable for patients¹⁵. In addition, fluctuations in plasma drug concentrations can lead to alternating periods of inadequate pain control and increased adverse effects. These challenges highlighted the need for a delivery system capable of providing sustained pain relief while improving patient comfort and treatment adherence.

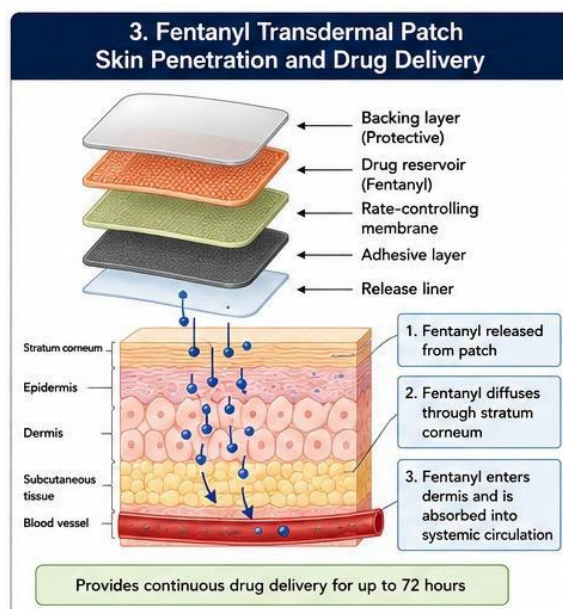


Fig. No. 3: Drug Delivery by Transdermal Patch.

4.1 Disease Context and Therapeutic Challenge: Chronic pain remains one of the most challenging conditions to manage in modern healthcare, particularly among cancer patients and individuals requiring long-term palliative care.

Fentanyl, a potent synthetic opioid analgesic, is widely used for the management of moderate to severe chronic pain because of its strong analgesic properties and rapid onset of action. However, conventional administration routes such as oral and intravenous delivery are associated with several limitations. When administered orally, fentanyl undergoes extensive first-pass metabolism in the liver, reducing its bioavailability and contributing to variability in therapeutic response among patients. Intravenous administration, although effective, often requires frequent dosing or continuous infusion, which may be inconvenient and uncomfortable for patients. In addition, fluctuations in plasma drug concentrations can lead to alternating periods of inadequate pain control and increased adverse effects. These challenges highlighted the need for a delivery system capable of providing sustained pain relief while improving patient comfort and treatment adherence.

4.2 Transdermal Delivery Technology: The fentanyl transdermal patch was developed as an innovative solution to overcome the limitations of traditional opioid administration. The system delivers fentanyl through the skin and directly into systemic circulation, thereby bypassing gastrointestinal absorption and hepatic first-pass metabolism. The patch consists of a drug-containing matrix or reservoir, an adhesive layer, and a protective backing membrane.^[16] After application to the skin, fentanyl gradually diffuses through the stratum corneum, which is the outermost protective layer of the skin. Once the drug reaches the deeper layers of the skin, it enters the bloodstream and provides prolonged analgesic effects. The transdermal route offers several advantages. Because fentanyl is continuously released at a controlled rate, relatively stable plasma drug concentrations can be maintained over an extended period. Most fentanyl patches are designed to provide effective analgesia for up to 72 hours following a single application. This controlled delivery profile reduces the peaks and troughs commonly observed with oral dosing and helps maintain consistent pain control.^[17]

4.3 Clinical Benefits and Therapeutic Outcomes: The introduction of fentanyl transdermal systems significantly improved pain management strategies for patients requiring long-term opioid therapy. One of the most important benefits is improved patient compliance. Instead of taking multiple doses each day, patients only need to replace the patch every three days, making treatment more convenient and less burdensome. Stable plasma concentrations achieved through transdermal delivery help reduce breakthrough pain episodes while minimising fluctuations in analgesic effect.

Many patients also report improved quality of life because the patch is non-invasive, discreet, and easy to use. The transdermal route is particularly beneficial for patients who have difficulty swallowing medications due to advanced disease, neurological disorders, or gastrointestinal complications. By avoiding the digestive system, the patch offers an effective alternative for maintaining long-term pain control in these populations.^[18]

4.4 Limitations and Future Perspectives

Despite its advantages, transdermal fentanyl therapy has several limitations. Drug delivery through the skin is influenced by factors such as skin thickness, hydration, age, and body temperature. Exposure to excessive heat from heating pads, hot baths, or fever may increase fentanyl absorption and potentially lead to opioid toxicity.

Skin irritation, allergic reactions, and patch adhesion problems are additional concerns that may affect treatment effectiveness. Furthermore, the delayed onset of action associated with transdermal delivery makes fentanyl patches unsuitable for acute pain management where rapid analgesia is required.^[19] Future developments in transdermal drug delivery are focused on overcoming the barrier properties of the skin. Technologies such as microneedle arrays, iontophoresis, electroporation, and nanoparticle-enhanced patches are being investigated to improve drug penetration and provide more precise control of drug release. Smart wearable systems capable of adjusting drug delivery in response to patient-specific physiological signals may further enhance the effectiveness of transdermal therapy.^[20]

5. Case Study 4: Controlled Release Drug Delivery – Metformin Extended-Release Tablets

5.1 Disease Context and Therapeutic Challenge: Type 2 Diabetes Mellitus (T2DM) is one of the most prevalent chronic metabolic disorders worldwide and represents a major public health challenge. The disease is characterised by insulin resistance, impaired glucose utilisation, and progressive pancreatic β -cell dysfunction. Effective long-term management requires sustained glycaemic control to prevent complications such as cardiovascular disease, nephropathy, neuropathy, and retinopathy. Metformin remains the first-line pharmacological treatment for T2DM because of its ability to reduce hepatic glucose production and improve insulin sensitivity. However, conventional immediate-release metformin formulations are associated with several drawbacks. Gastrointestinal adverse effects including nausea, diarrhoea, abdominal discomfort, and bloating are frequently reported, particularly during the initiation of therapy.^[21]

In addition, immediate-release formulations often require multiple daily doses because of the relatively short elimination half-life of the drug. Frequent dosing schedules may reduce patient adherence and compromise long-term treatment outcomes.^[22]

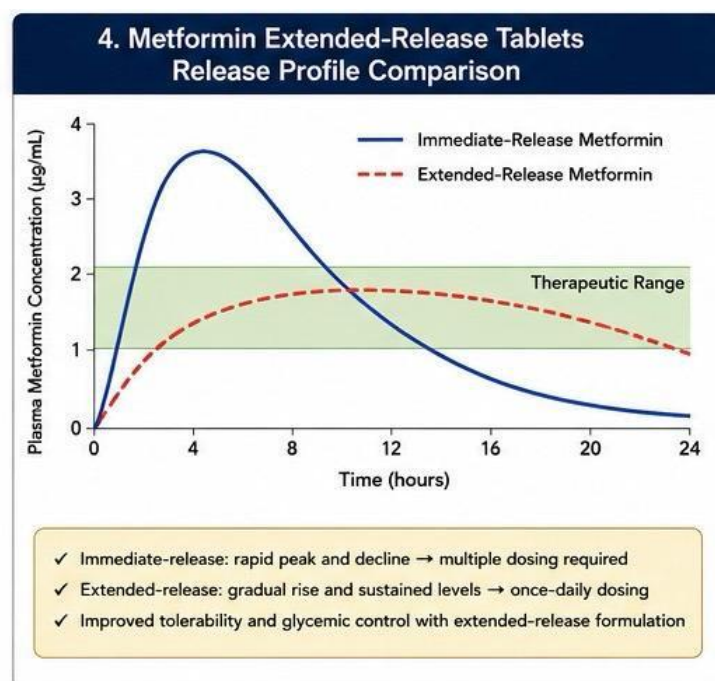


Fig. No. 4: Metformin ER Tablet: Release Profile Graph.

5.2 Controlled Release Technology and Mechanism: To address these limitations, extended-release (ER) formulations of metformin were developed using controlled-release drug delivery technologies. Most metformin ER products utilise hydrophilic polymer matrices composed of materials such as hydroxypropyl methylcellulose (HPMC).

When exposed to gastrointestinal fluids, these polymers absorb water and form a gel-like barrier around the tablet.^[23]

The gel layer controls the movement of drug molecules from the tablet into the surrounding environment. As the matrix gradually hydrates and swells, metformin is released slowly over an extended period. This mechanism enables sustained drug delivery for up to 24 hours following administration. The controlled-release profile reduces rapid peaks in plasma concentration and provides a more consistent therapeutic effect throughout the day. By maintaining steady drug levels, the formulation improves tolerability and minimises fluctuations in glucose control.^[24]

5.3 Clinical Benefits and Therapeutic Outcomes: Clinical studies have consistently demonstrated the advantages of extended-release metformin formulations. One of the most significant benefits is the reduction in gastrointestinal adverse effects compared with immediate-release products. The slower release of the drug decreases local concentrations in the gastrointestinal tract, thereby improving tolerability. The once-daily dosing regimen also contributes to improved medication adherence. Patients are generally more likely to follow treatment recommendations when dosing schedules are simple and convenient.^[25] Improved adherence is particularly important in chronic diseases such as diabetes, where long-term therapeutic success depends heavily on consistent medication use. Studies have shown that metformin ER provides glycaemic control comparable to or better than immediate-release formulations while offering a superior tolerability profile. These benefits have made extended-release metformin a preferred option for many patients who experience gastrointestinal intolerance with conventional therapy.^[26]

5.4 Limitations and Future Perspectives: Although controlled-release formulations offer significant advantages, they are not without limitations. The rate of drug release can be influenced by gastrointestinal transit time, pH variations,

and patient-specific physiological factors. Improper tablet handling, such as crushing or chewing, may disrupt the controlled-release mechanism and result in unintended rapid drug release²⁴. Researchers are currently exploring advanced gastro-retentive delivery systems designed to prolong the residence time of metformin within the stomach and upper gastrointestinal tract. Floating tablets, mucoadhesive systems, and expandable dosage forms are among the approaches being investigated. Another promising area involves osmotic-controlled drug delivery systems that can provide highly predictable release profiles independent of gastrointestinal conditions. These next-generation technologies may further improve therapeutic consistency, patient adherence, and overall diabetes management outcomes.^[25,26]

6. Case Study 5: Lipid Nanoparticle-Based mRNA Vaccines for COVID-19

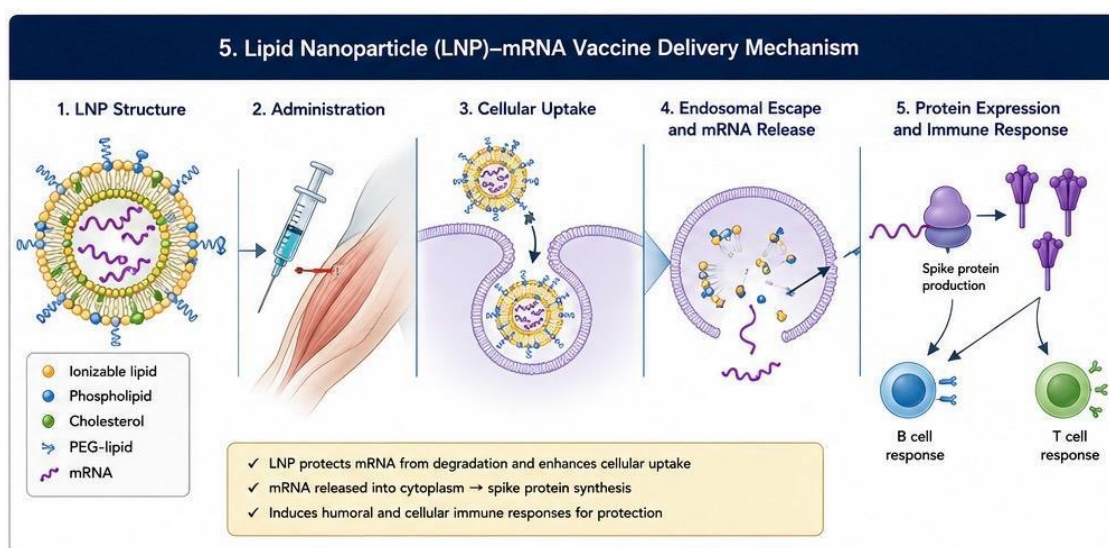


Fig. No. 5: Lipid Nanoparticle-mRNA Vaccine Delivery Mechanism.

6.1 Disease Context and Therapeutic Challenge: The emergence of Coronavirus Disease 2019 (COVID-19) created an unprecedented global healthcare crisis and highlighted the urgent need for rapid vaccine development. Traditional vaccine technologies, such as live-attenuated or inactivated vaccines, often require extensive development and manufacturing timelines. During a rapidly spreading pandemic, these timelines can significantly delay public health responses. Messenger RNA (mRNA) vaccines emerged as a revolutionary alternative because they can be designed and manufactured quickly once the genetic sequence of a pathogen becomes available. Instead of introducing a weakened or inactivated pathogen into the body, mRNA vaccines deliver genetic instructions that enable host cells to produce a specific viral protein. The immune system then recognises this protein as foreign and develops protective immunity.

Despite their potential, mRNA molecules face several challenges. They are highly unstable, susceptible to enzymatic degradation, and unable to efficiently cross cell membranes because of their large size and negative charge. Therefore, an effective delivery system was essential for the successful clinical application of mRNA-based therapeutics.^[27]

6.2 Lipid Nanoparticle Technology and Mechanism: Lipid nanoparticles (LNPs) provided the breakthrough solution that enabled the successful delivery of mRNA vaccines. These nanoparticles serve as protective carriers that encapsulate fragile mRNA molecules and facilitate their transport into target cells. The LNP systems used in the Pfizer-BioNTech (BNT162b2) and Moderna (mRNA-1273) vaccines consist of four major lipid components: ionisable lipids,

phospholipids, cholesterol, and polyethylene glycol (PEG)-modified lipids. Each component performs a specific function in ensuring vaccine stability and delivery efficiency²⁸. The ionisable lipid plays a particularly important role by binding to the negatively charged mRNA during formulation and assisting with endosomal escape after cellular uptake.

Once inside the cell, the mRNA is released into the cytoplasm, where it directs the synthesis of the SARS-CoV-2 spike protein. This protein subsequently stimulates both humoral and cellular immune responses, resulting in protective immunity against the virus. The use of lipid nanoparticles not only protects mRNA from degradation but also significantly enhances cellular uptake, making large-scale mRNA vaccination feasible for the first time in medical history.

6.3 Clinical Benefits and Global Impact: The success of lipid nanoparticle-based mRNA vaccines represents one of the most significant achievements in pharmaceutical and biomedical science. Clinical trials demonstrated remarkably high efficacy rates against symptomatic COVID-19 infection. The Pfizer-BioNTech vaccine reported approximately 95% efficacy, while the Moderna vaccine demonstrated efficacy exceeding 94%. Beyond their effectiveness, mRNA vaccines showcased unprecedented development speed. Within a year of the publication of the viral genome sequence, safe and effective vaccines were developed, clinically evaluated, and authorised for emergency use. This achievement highlighted the flexibility and scalability of mRNA-LNP technology. The success of these vaccines extended beyond pandemic management. Researchers recognised that the same platform could potentially be adapted for various applications, including cancer immunotherapy, genetic disorders, infectious diseases, and personalised medicine.

Consequently, lipid nanoparticle technology has become a major focus of pharmaceutical innovation worldwide.^[29]

6.4 Limitations and Future Perspectives: Although highly successful, current mRNA-LNP vaccines are associated with certain limitations. One major challenge is storage and distribution. Early vaccine formulations required ultra-low-temperature storage, creating logistical difficulties, particularly in resource-limited settings. Another concern involves potential immune reactions against some lipid nanoparticle components, particularly PEG-containing materials.

Researchers are also investigating the biodistribution of LNPs to ensure precise targeting and minimise off-target effects. Future developments aim to create thermostable formulations that can be stored at standard refrigeration or room temperatures. Scientists are additionally exploring targeted LNP systems capable of delivering genetic material to specific organs and tissues. Advances in self-amplifying mRNA technology may further reduce the required vaccine dose while maintaining strong immune responses. These innovations are expected to expand the therapeutic applications of mRNA delivery systems far beyond infectious disease prevention.^[30]

7. Comparative Analysis of Clinically Successful NDDS Technologies

7.1 Comparative Evaluation: The five case studies discussed in this review demonstrate how different NDDS technologies address distinct therapeutic challenges while sharing a common objective: improving the safety, efficacy, and patient acceptability of drug therapy. Liposomal delivery systems such as Doxil® primarily focus on reducing toxicity and improving tumour targeting. Albumin-bound nanoparticles like Abraxane® enhance the solubility and delivery of poorly water-soluble drugs while eliminating harmful formulation excipients. Transdermal fentanyl patches provide sustained systemic drug delivery through a non-invasive route and improve patient adherence. Extended-release metformin formulations offer controlled drug release and improved gastrointestinal tolerability, making long-

term disease management more convenient. Finally, lipid nanoparticle-based mRNA vaccines demonstrate the ability of NDSS to enable entirely new therapeutic modalities that would otherwise be impossible. Despite their differences, all these technologies illustrate the importance of formulation science in enhancing therapeutic performance and expanding clinical treatment options.

8. Future Perspectives of Novel Drug Delivery System

8.1 Artificial Intelligence in Drug Delivery Design: Artificial intelligence (AI) is rapidly transforming pharmaceutical research and development. Machine learning algorithms can analyse large datasets containing information on drug properties, formulation parameters, biological interactions, and clinical outcomes. These tools can help researchers identify optimal delivery systems more efficiently than traditional trial-and-error approaches. AI-driven formulation design may significantly reduce development timelines while improving the precision of nanoparticle engineering, targeted delivery strategies, and personalised treatment approaches.

8.2 Stimuli-Responsive Drug Delivery Systems: Future drug delivery systems are expected to become increasingly intelligent and responsive. Stimuli-responsive carriers can release therapeutic agents only when exposed to specific internal or external triggers. Examples include pH-sensitive systems that release drugs within acidic tumour environments, enzyme-responsive carriers activated by disease-specific biomarkers, and temperature-sensitive formulations designed for localised treatment. Such technologies offer the possibility of highly selective drug release with minimal exposure of healthy tissues, thereby improving therapeutic outcomes and reducing adverse effects.^[2]

8.3 Personalised Medicine and 3D Printing: The growing field of personalised medicine aims to tailor treatment strategies to individual patient characteristics. Advances in pharmacogenomics and biomarker analysis may enable the development of patient-specific drug delivery systems that account for genetic, physiological, and disease-related differences. Three-dimensional (3D) printing technology further supports this vision by enabling the production of customised dosage forms with specific release profiles, strengths, and drug combinations. Such innovations may revolutionise pharmaceutical manufacturing and improve treatment individualisation.

8.4 Theragnostic and Multifunctional Nanomedicine: Theragnostic systems combine diagnostic and therapeutic functions within a single platform. These advanced systems can simultaneously deliver drugs and monitor treatment responses through imaging technologies. The integration of diagnosis and therapy has the potential to improve disease monitoring, optimise treatment decisions, and support precision medicine. Researchers are also investigating multifunctional nanoparticles capable of targeted delivery, controlled release, imaging, and real-time therapeutic monitoring. Such systems represent the next generation of advanced pharmaceutical technologies³.

CONCLUSION

Novel Drug Delivery Systems have fundamentally transformed modern pharmaceutical therapy by overcoming many of the limitations associated with conventional dosage forms. Through innovations such as liposomes, nanoparticles, transdermal systems, controlled-release formulations, and lipid nanoparticles, NDSS has improved drug targeting, enhanced therapeutic efficacy, reduced toxicity, and increased patient compliance. The clinical success of Doxil®, Abraxane®, transdermal fentanyl patches, extended-release metformin, and lipid nanoparticle-based mRNA vaccines clearly demonstrates the practical value of advanced drug delivery technologies in addressing real-world therapeutic challenges. These products have not only improved patient outcomes but have also expanded the possibilities of

pharmaceutical treatment. Although challenges related to manufacturing complexity, cost, scalability, and regulatory considerations remain, ongoing advancements in nanotechnology, artificial intelligence, personalised medicine, and smart delivery systems continue to drive the field forward. As research progresses, NDDS is expected to play an increasingly important role in precision medicine and next-generation therapeutics, ultimately contributing to safer, more effective, and more patient-centred healthcare solutions.

REFERENCES

1. Allen TM, Cullis PR. Liposomal drug delivery systems: from concept to clinical applications. *Adv Drug Deliv Rev*, 2013; 65(1): 36–48.
2. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. *Nat Nanotechnol*, 2007; 2(12): 751–760.
3. Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress, challenges and opportunities. *Nat Rev Cancer*, 2017; 17(1): 20–37.
4. Gabizon A, Shmeeda H, Barenholz Y. Pharmacokinetics of pegylated liposomal doxorubicin: review of animal and human studies. *Clin Pharmacokinet*, 2003; 42(5): 419–436.
5. Gradishar WJ, Tjulandin S, Davidson N, Shaw H, Desai N, Bhar P, et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel. *J Clin Oncol*, 2005; 23(31): 7794–7803.
6. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *N Engl J Med*, 2020; 383(27): 2603–2615.
7. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med*, 2021; 384(5): 403–416.
8. Barenholz Y. Doxil®—The first FDA-approved nano-drug: lessons learned. *J Control Release*, 2012; 160(2): 117–134.
9. O'Brien ME, Wigler N, Inbar M, Rosso R, Grischke E, Santoro A, et al. Reduced cardiotoxicity and comparable efficacy of pegylated liposomal doxorubicin. *Ann Oncol*, 2004; 15(3): 440–449.
10. Torchilin VP. Recent advances with liposomes as pharmaceutical carriers. *Nat Rev Drug Discov*, 2005; 4(2): 145–160.
11. Desai N, Trieu V, Yao Z, Louie L, Ci S, Yang A, et al. Increased antitumor activity and transport of albumin-bound paclitaxel nanoparticles. *Clin Cancer Res*, 2006; 12(4): 1317–1324.
12. Elsadek B, Kratz F. Impact of albumin on drug delivery—new applications on the horizon. *J Control Release*, 2012; 157(1): 4–28.
13. Von Hoff DD, Ervin T, Arena FP, Chiorean EG, Infante J, Moore M, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med*, 2013; 369(18): 1691–1703.
14. Farokhzad OC, Langer R. Impact of nanotechnology on drug delivery. *ACS Nano*. 2009;3(1):16–20.
15. Prausnitz MR, Langer R. Transdermal drug delivery. *Nat Biotechnol*, 2008; 26(11): 1261–1268.
16. Drobnick RK, Svensson CK. Therapeutic drug monitoring in saliva: an update. *Clin Pharmacokinet*, 1992; 23(5): 365–379.
17. Stanley TH. The fentanyl story. *J Pain*, 2014; 15(12): 1215–1226.
18. Donner B, Zenz M, Tryba M, Strumpf M. Direct conversion from oral morphine to transdermal fentanyl. *Pain*, 1996; 64(3): 527–534.
19. Guy RH. Transdermal drug delivery revisited. *Int J Pharm*, 2010; 398(1–2): 1–4.

20. Ita K. Transdermal drug delivery: progress and challenges. *J Drug Deliv Sci Technol*, 2015; 24(3): 245–250.
21. Bailey CJ, Turner RC. Metformin. *N Engl J Med*, 1996; 334(9): 574–579.
22. DeFronzo RA, Buse JB, Kim T, Burns C, Skare S, Baron A, et al. Once-daily delayed-release metformin lowers plasma glucose. *Diabetes Care*, 2016; 39(11): 1985–1991.
23. Colombo P, Bettini R, Santi P, Peppas NA. Swellable matrices for controlled drug delivery. *Pharm Sci Technol Today*, 2000; 3(6): 198–204.
24. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery systems. *Expert Opin Drug Deliv*, 2006; 3(2): 217–233.
25. Blonde L, Dailey GE, Jabbour SA, Reasner CA, Mills DJ. Gastrointestinal tolerability of extended-release metformin tablets. *Clin Ther*, 2004; 26(4): 565–573.
26. Fujioka K, Brazg RL, Raz I, Bruce S, Joyal S, Swanink R. Efficacy and safety of once-daily extended-release metformin. *Diabetes Care*, 2003; 26(3): 683–688.
27. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines—a new era in vaccinology. *Nat Rev Drug Discov*, 2018; 17(4): 261–279.
28. Hou X, Zaks T, Langer R, Dong Y. Lipid nanoparticles for mRNA delivery. *Nat Rev Mater*, 2021; 6(12): 1078–1094.
29. Cullis PR, Hope MJ. Lipid nanoparticle systems for enabling gene therapies. *Mol Ther*, 2017; 25(7): 1467–1475.
30. Reichmuth AM, Oberli MA, Jaklenec A, Langer R, Blankschtein D. mRNA vaccine delivery using lipid nanoparticles. *Nanomedicine*, 2016; 11(5): 543–555.