

# Exploring Nanoparticle Carriers: A Comprehensive Review of Drug Release Mechanisms for Cancer, Cardiovascular Diseases, and Diabetes

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## Abstract

This study provides a comprehensive examination of drug delivery systems, focusing on nanoparticles derived from chitosan, silica, and poly(lactic-co-glycolic acid) (PLGA) for cancer therapy. Nanoparticle-based Drug Delivery Systems (NDDSs) are emerging as promising options for treating cardiovascular diseases due to their enhanced efficiency and extended half-life, despite ongoing concerns about cellular toxicity. For diabetes, transdermal systems have surfaced as an effective treatment method. This review offers a holistic perspective on the advancements and challenges of NDDSs, emphasizing their applications in managing cancer, cardiovascular diseases, and diabetes.

**Keywords:** Drug Delivery, Carrier, Nano Particles

## 1.Introduction

Drug carriers are biocompatible instruments used in nutraceutical, pharmaceutical, and cosmetic applications for the transportation of molecules. It is anticipated that the worldwide market for sophisticated drug delivery systems, encompassing drug carriers, will expand from \$148 billion in 2015 to \$310 billion by 2025. The necessity of secure and efficient vaccines has been brought to light by the COVID-19 pandemic.

Drug carriers enhance the selectivity, bioavailability, and efficacy of pharmaceuticals by efficiently delivering and safeguarding them. A drug carrier is a specialised mechanism that travels throughout the body carrying medication. This could be a liposome, nanoparticle, or another kind of delivery system. Medication carriers aid in improving the solubility, targeting particular tissues, stabilising the medication, and controlling its release, all of which contribute to improved therapeutic efficacy. Microcapsules, microspheres, and lipid-based vesicles can prevent drug leakage and deliver drugs to healthy tissues, reducing side effects. Drug delivery systems are designed at the nanometer and micrometer levels to have specific properties like site-specificity, lifetime, and responsiveness to external stimuli. These nanosystems are able to improve the stability, solubility, and uptake of drugs, increasing their safety and efficacy [1-2-3].

Drug delivery systems have limitations like restricted efficacy and lack of selectivity, which can be addressed by controlled drug delivery systems that target cancer cells and reduce toxicity in normal cells. Three types of nanoparticles used in cancer treatment include chitosan, silica, and PLGA [4].

Cardiovascular illnesses represent a significant public health concern, and drug delivery systems utilising nanoparticles may enhance the solubility, stability, and absorption of medications for these illnesses. But as nanomaterials are used more often, safety concerns have grown, necessitating a careful analysis of their impact on human health [5].

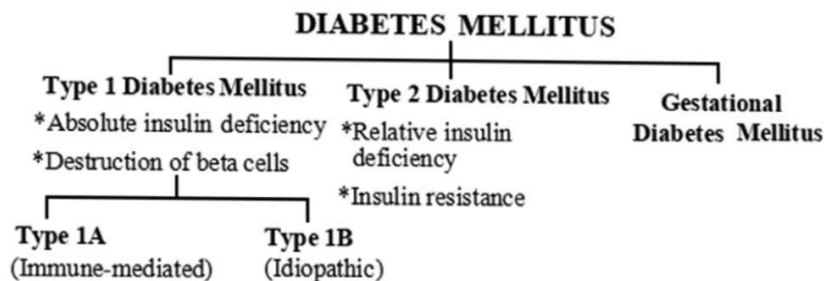
Diabetes is a chronic illness that can be lethal if improperly treated. It is anticipated that the current diabetes population would rise from 415 million to 642 million by 2040. In order to treat type 2 diabetes, blood sugar-lowering medications must be taken. [6].

## 2. Transdermal Delivery

Drug delivery by skin penetration, or transdermal distribution, can be done in an active or passive way. While the active strategy uses heat, ultrasound, electroporation, laser ablation, microoperation, or an electric field to artificially produce penetration, the passive approach relies on gradient diffusion. Delivery Subcutaneous involves using a needle to administer a certain medication.

However, there are instances in which the needle is not utilised. Rather, a gun that injects medications quickly into the subcutaneous tissue is used to provide the medication. The administration of insulin for the treatment of both type 1 and type 2 diabetes is a prime illustration of the subcutaneous delivery mechanism.

Pellet implantation, which involves introducing medication in pellet form through a cannula, is utilised in certain situations. With this approach, medication is released sustainably throughout the week and fewer doses are required. Testosterone is a prime example of a medication administered by pellet implantation (figure 1) [7-8-9].



**Figure1.** Classification of diabetes mellitus. Association AD. Diagnosis and classification of diabetes [10].

### 2.1. Micropumps and patches

Insulin is delivered using micropumps to treat type 1 diabetes.

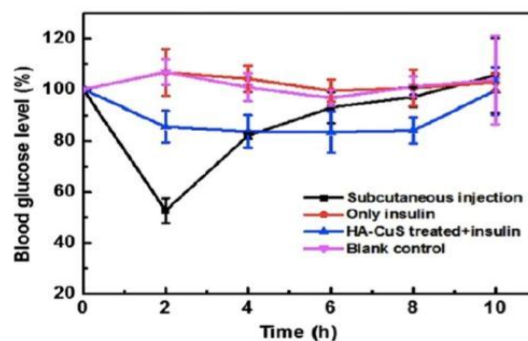
With this technique, tiny, computerised pumps are designed to dispense medication at specific rates, either continuously or in pulses. The glucose level sensors that are placed to the skin must communicate with these pumps. The

pump modifies the amount of insulin delivered to the body by measuring the glucose concentration. The insulin delivered by the pump is increased if the glucose level above 180 mg/dL. On the other hand, insulin delivery is halted until the glucose level returns to an ideal range if it drops below 60 mg/dL. In conclusion, these micropumps help manage type 1 diabetes by automating the supply of insulin based on realtime monitoring of the user's glucose levels (figure 2) [11].

Figure 2 shows the blood glucose levels of diabetic mice across four different groups:

1. Positive control: Mice received subcutaneous insulin injections.
2. Untreated + insulin: Diabetic mice received insulin treatment.
3. HA-CUs treated + NIR laser + insulin: Diabetic mice were treated with hyaluronic acid-coated upconversion nanoparticles (HA-CUs), exposed to near-infrared (NIR) laser light, and given insulin.
4. Blank control: Untreated diabetic mice.

The results demonstrate the effects of the different treatment approaches on blood glucose regulation in the diabetic mouse model. The data provides insights into the potential of the HA-CUs and NIR laser combination, along with insulin, to effectively manage blood glucose levels in comparison to insulin treatment alone or no treatment. This information was originally published in a 2017 paper, with permission granted for the reprinting of the relevant figure and data in the current context [12].



**Figure 2.** The study examined the blood glucose levels of diabetic mice across four different groups [12].

### 3. Nano particles

Applications for nanoparticles include radiation therapy, gene therapy, cancer therapy, and virus treatment.

They are frequently used to administer vaccinations, proteins, antibiotics, and vitamins.

These medications based on nanoparticles have the potential to get beyond a number of obstacles, including low tissue absorption, poor bioavailability, and drug loss during delivery to target cells.

Modern medicine has made it possible to improve drug delivery, which has resulted in the creation of innovative nano-robots that can treat cancer.

The development of more precise and potent medicines is now a possibility thanks to these technical advances. Nanoparticles derived from natural polymeric materials, such as chitosan; inorganic materials, silica; and synthetic materials, polylactide-co-glycolic acid (PLGA) nanoparticles, are employed in the treatment of cancer (figure 3) [13-14-15-16].

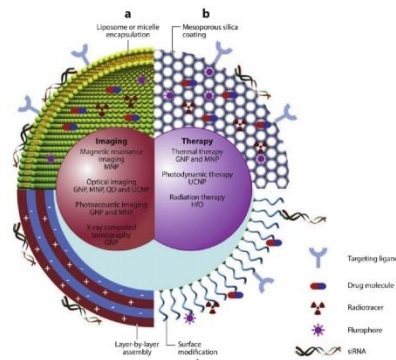


figure3.schematic nanoparticles[17].

These diverse nanoparticle building blocks can be integrated together to engineer multifunctional nanoparticles with enhanced capabilities compared to individual nanoparticle types.

The combination of these nanomaterials enables the integration of various functionalities, such as optical, magnetic, catalytic, and sensing properties, into a single multifunctional nanoparticle platform. The schematic diagram illustrates the potential to create highly sophisticated nanoparticle systems by strategically assembling and integrating different nanomaterial components. This represents an important advancement in the development of advanced nanomaterials with broad applications in fields like biomedical engineering, catalysis, energy, and electronics[17].

### 3.1. Applications of chitosan nanoparticles in drug delivery

The potential of chitosan nanoparticles in cancer therapy has been extensively researched.

Through a variety of methods, they allow for the targeted delivery of medications to particular organs and tissues:

1. Passive targeting: Chitosan nanoparticles can preferentially aggregate in tumour tissues because of the enhanced permeability and retention (EPR) effect, which is caused by leaky vasculature and inadequate lymphatic drainage in tumours.
2. Active targeting: By adding targeting ligands that attach to receptors overexpressed on cancer cells, chitosan nanoparticles can be engineered to actively seek out and transport medications to the tumour location.
3. Stimuli-sensitive targeting: Chitosan nanoparticles' characteristics can be engineered to react to particular stimuli, including temperature or pH changes, enabling them to discharge their payload at the intended site inside the body.

Chitosan nanoparticles have demonstrated potential as an efficient drug delivery system for cancer treatment due to their various targeting mechanisms, which allow for better delivery of therapeutic drugs to the tumour site.[18].

### 3.2. Applications of PLGA nanoparticles in cancer treatment

Although the enhanced permeability and retention (EPR) impact of passive distribution of PLGA nanoparticles has been investigated for the treatment of cancer, the result is frequently insufficient medication delivery to tumours. Consequently, a lot of PLGA nanoparticle applications in cancer therapy make use of active targeting techniques. PLGA nanoparticles are frequently surface-attached with targeting ligands to facilitate selective binding to receptors overexpressed on cancer cells or tumour blood arteries. Natural polysaccharide hyaluronic acid (HA) binds to CD44 receptors, which are overexpressed in certain malignancies and can function as a targeting moiety. Benefits of HA include its non-toxicity, biocompatibility, biodegradability, and lack of immunogenicity. One such study used HA-coated PLGA nanoparticles to treat triple negative Breast cancer by delivering paclitaxel.

For maximum drug loading and encapsulation efficiency, formulation parameters like PVA concentration and sonication time were tuned. Because of interactions between the HA and CD44 receptors, the HA coating enhanced drug release and cellular absorption in comparison to uncoated PLGA nanoparticles. Using outside stimuli, like as magnetic fields, to direct the nanoparticles to the tumour location is an additional strategy for active targeting. To break through the blood-

brain barrier, for example, dual Targeted magnetic PLGA nanoparticles have been studied for the treatment of gliomas[19-20-21].

### 3.3. Future of nanoparticles as drug delivery systems

Given all of its benefits over conventional distribution methods, nanoparticles appear to have a bright future as medication delivery systems. Nevertheless, further investigation via in vivo investigations and clinical trials is required to comprehend their toxicity and enduring consequences.

One area of interest is surface modification of nanoparticles, where polyethylene glycol is a commonly used option to lengthen the duration of circulation. Imitating natural cell membranes with cell membrane-coated nanoparticles is another exciting strategy that can enhance biodistribution and lessen immunological responses. The field of developing multifunctional nanoparticles is expanding due to the increased demands in medicine, including image-guided drug delivery for cancer treatment. This method tracks the behaviour of nanoparticles inside the body by combining them with imaging modalities such as MRI [22-23-24].

### 3.4. Liposomes

Among the most popular kinds of drug delivery systems, liposomes are used in nutraceuticals, cosmetics, and medicines. These spherical vesicles are made up of one or more membranes with phospholipid bilayers. Liposomes have the capacity to encapsulate lipophilic medications within the phospholipid bilayer and hydrophilic drugs within their inner core. For their anticancer effects, medications like daunorubicin and amphotericin are frequently delivered to target cells in liposome form. The two primary benefits of employing liposomes are lower toxicity and improved stability of the medicine that is encapsulated. Because target cell membranes and liposomes have comparable lipid compositions, liposomes can also fuse with them. Liposomes frequently have better pharmacokinetics and a greater therapeutic index when compared to other drug carriers. They are non-pyrogenic, non-antigenic, biodegradable, and biologically inert.

However, there are a number of difficulties associated with liposome synthesis, including low repeatability and high cost. In conclusion, despite certain difficulties in their large-scale production, liposomes are a flexible drug delivery system that can enhance the safety and effectiveness of a variety of therapeutic agents, especially in the treatment of cancer [25-26].

## 4. natural drug carriers

In addition to synthetic drug carriers, natural drug carriers are accessible and naturally occur in the human body. For example, neutrophils deliver therapeutic medicines to regions impacted by acute inflammation. Furthermore, lymphocytes are generated to facilitate the transfer of macromolecules such as DNA; drugs are loaded into erythrocytes to form nanoerythrocytes, commonly referred to as "golden eggs," which offer ample space for drug incorporation and accumulation; and monoclonal antibodies are generated by a single clone and specifically target an epitope [27-28-29].

### 4.1. Exosome

Exosomes are comparable to other forms of liquid-based, lyotropic liquid crystals seen in natural systems, with highly organised nanostructures. They are membrane-bound extracellular vesicles made in the endosomal compartments of the majority of eukaryotic cells, although they lack a distinct backbone. These vesicles are capable of carrying genetic material, proteins, and lipids.

They are important because they can offer prognostic information regarding the spread of carcinoid tumours. Exosomes are thought to be a means by which the human body communicates with its cells. An increased and uncontrolled amount of exosomes produced by a cancerous cell can lead to the spread of tumors [30].

## 5. Therapeutic window

The idea of the therapeutic window has been connected to the effectiveness and security of the medication carriers. The y and X axes of a diagram, which represent the drug concentration and the time variable, respectively, outline the therapeutic window. During administration, the concentration of medicines rises with time. In addition, the concentration profile between the upper and lower concentration limits needs to be specified (figure 4).

The condition above which a toxic effect is anticipated and which is harmful to both the target tissues and other cells is shown by the graph on the right. Towards the left, the graph indicates the safe level below which the target cells are not harmed. Insulin patches have been created using microneedles and a variety of materials. Furthermore, factors. Variations in needle length, diameter, and excipients are studied in order to identify how best to modify the method and obtain the best results.

Insulin injections and oral medications are currently the two most often prescribed treatments for diabetes. Even though there is a lot of research being done on microneedles for the mass manufacture of insulin transdermal patches. Since there is still study being done on many pharmacological features, this system has not yet been widely implemented.

Figure 4

demonstrates (a) the average drug concentration over the course of the medication's release.

$C_{min}$  is the lowest drug concentration necessary to provide a therapeutic effect, while  $C_{max}$  is the highest drug concentration above which there are harmful effects on target tissues.

(b) following a single medication administration, two pulsed drug release phases.

The term "end of first release" refers to the point at which the first released dose's effects wear off and a fresh external stimulus is required to initiate the subsequent release. (c) drug release that is regulated by two different mechanisms: diffusion control at first, and erosion control later.

The typical drug release behaviour from longcirculating liposomes targeted to certain cells is seen in (d). The long term objective is to keep the medication concentration within the therapeutic window. All things considered, these illustrations offer a qualitative grasp of various drug delivery profiles and the idea of the therapeutic window that is, the range of drug concentrations that result in the intended therapeutic impact without posing a hazard[31].

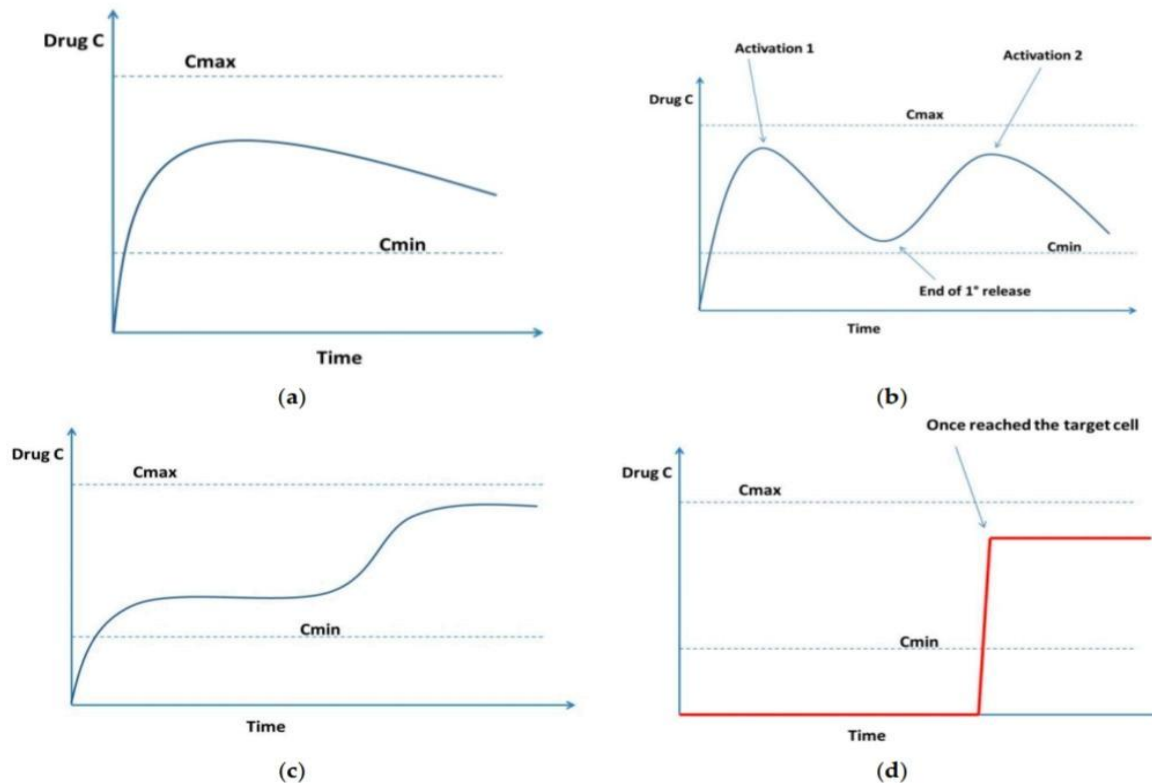


Figure4. shows the typical drug concentration over time during drug release[31].

## 6. conclusion

Drug carriers have emerged as a crucial element in the pharmaceutical industry, driven by several key factors. Primarily, they enhance the stability and solubility of drugs, which is fundamental for their efficacy. Additionally, drug carriers improve the absorption and controlled release of medications within the human body, ensuring that the therapeutic compounds reach their intended targets more efficiently. This targeted delivery significantly reduces side effects and optimizes the pharmacokinetic and pharmacodynamic properties of drugs, thereby increasing their overall effectiveness. The review indicates that Poly(lactic-co-glycolic acid) (PLGA) carriers demonstrate superior suitability compared to other types of carriers. This superiority stems from the ability of PLGA polymers to be



precisely engineered for controlled timing, release rates, and targeted delivery of drugs. These attributes make PLGA-based systems particularly advantageous in enhancing the therapeutic outcomes of various treatments. Finally, the advancements in drug carrier technology, especially with PLGA polymers, hold great promise for future developments in drug delivery systems, offering more efficient, targeted, and safe therapeutic options. Continued research and innovation in this field are essential to fully realize the potential benefits of these advanced drug delivery systems in clinical practice.

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