



The Evolution of Drug Delivery Systems: From Conventional Dosage to Novel Systems

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ABSTRACT

The efficacy of pharmacotherapy predominantly relies on the delivery technique employed to transport medications to their target site of action. Traditional drug delivery systems frequently result in suboptimal therapeutic results due to non-specific dispersion, fast degradation, frequent administration, and heightened systemic side effects. These issues have resulted in the advancement of Novel Drug Delivery Systems (NDDS). Nanoparticle drug delivery systems are engineered to augment drug bioavailability, optimize therapeutic efficacy, and provide controlled or targeted drug release, all while minimizing toxicity. Advanced carrier systems, including nanoparticles, liposomes, microspheres, and niosomes, enhance medication protection, stability, and targeted delivery. This study elucidates the concepts, classifications, benefits, and therapeutic applications of NDDS, underscoring their significant significance in augmenting drug efficacy, minimizing adverse effects, and promoting patient adherence in contemporary pharmacological therapy.

Keywords: Evolution of Drug Delivery Systems, Conventional Dosage to Novel Systems

INTRODUCTION

The strategy of medicine intake can substantially influence its effectiveness. Few pharmaceuticals possess an ideal concentration range that yields maximal efficacy, while levels exceeding or falling short of this range may result in toxicity or lack therapeutic value entirely [1].

In traditional drug delivery systems like oral intake or intravenous injections, the medication is disseminated throughout the body via systemic blood circulation. For the majority of medicinal medicines, only a minimal fraction of the medication attains the targeted organ or tissue [2].

The sluggish advancement in the effectiveness of severe disease treatments indicates an increasing necessity for a multidisciplinary strategy in the administration of medicines to tissue targets. These novel tactics, commonly referred to as drug delivery systems (DDS), are found on interdisciplinary methodologies that integrate polymer science, pharmaceutics, and molecular biology [3].

Innovative drug delivery systems provide medication stability, regulated release, targeted distribution, and improved bioavailability through the utilization of technologies such as nanoparticles, liposomes, patches, or implantable devices. These innovations enhance not only therapeutic outcomes but also patient happiness and adherence [1].

Various carriers are utilized for drug delivery, including soluble polymers, microparticles composed of insoluble or biodegradable natural and synthetic polymers, microcapsules, cell ghosts, lipoproteins, liposomes, and micelles [4].

Nanoparticles are characterized as particulate dispersions or solid particles of between 10 and 1000 nm in size. The medicine is dissolved, entrapped, encapsulated, or affixed to a nanoparticle matrix [5].

Targeted drug delivery is an advanced drug delivery technology that administers medication to certain tissues while minimizing its concentration in other areas. The targeted medication delivery method is favored over traditional drug delivery systems for three primary reasons [6].

Conventional drug delivery systems

The Conventional Drug Delivery System is the framework that utilizes standard methods for administering drugs into the body [7].

Conventional Drug Delivery System includes methods and formulations that utilize known procedures, primarily concentrating on oral, buccal, injectable, topical, inhalation, and rectal administration routes [8]. Each of these approaches' functions according to fundamental principles of pharmacokinetics and pharmacodynamics, guaranteeing that the medication is released, absorbed, and utilized by the body in a predictable manner as presented in Figure 1.

Limitations of Conventional Drug Delivery Systems

- Regular administration of the medication is essential.
- The standard dosage form is administered at a predetermined frequency and dosage.
- Patient adherence may be adversely affected by a reduced half-life and an increased likelihood of drug dosage adjustments.
- Attaining the steady state condition results from the peak valley plasma profile.
- Categories of Traditional Delivery Systems Conventional Drug Delivery System are classified according to the method of administration [9].

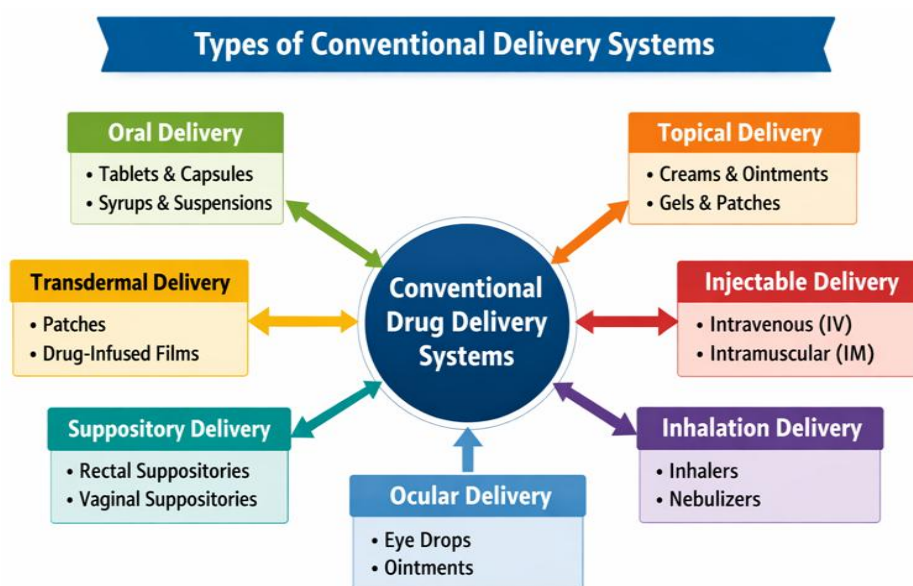


Figure 1: Types of conventional drug delivery systems

Novel drug delivery systems

A Novel Drug Delivery System (NDDS) is defined as a unique technique that integrates advanced development, formulations, technologies, and procedures for the administration of pharmaceutical chemicals in the body to safely attain the intended pharmacological effects [10]. A novel drug delivery system has been designed to surpass conventional medication administration methods to fulfil the requirements of the healthcare profession [11].

Novel drug delivery methods may encompass those founded on physical mechanisms and those grounded on biological principles. Physical mechanisms, also known as controlled drug delivery systems, encompass osmosis, diffusion, erosion, dissolution, and

electro-transport, whilst biochemical techniques comprise monoclonal antibodies, gene therapy, vector systems, polymer drug conjugates, and liposomes [12].

Diverse drug delivery systems have been created to minimize drug loss, mitigate adverse side effects, enhance bioavailability of medication, and promote drug accumulation in the targeted bio-zone[13].

These systems can be characterized as Control Drug Delivery Systems or Targeted Drug Delivery Systems [14].

Sustained or controlled drug delivery systems administer medication at a predetermined rate, facilitating prolonged or constant (zero-order) release, thereby maintaining therapeutically effective concentrations in the circulation.

Targeted drug delivery facilitates pharmacological activity by carriers that utilize either passive or active diffusion, or a self-programmed mechanism that identifies receptors at the designated spot. The therapeutic advantages of these systems encompass enhanced drug efficacy, targeted delivery, reduced toxicity or adverse effects, and improved patient adherence [15].

The carrier-based drug system is a method that utilizes certain agents to improve the selectivity, effectiveness, and safety of drug delivery. These carriers can enhance the solubility, stability, and delivery of medicines to specific sites, resulting in more efficacious therapeutic outcomes [16].

Since its inception, NDDS has experienced numerous modifications, including the application of extracellular matrices, nanoparticles, microencapsulation, epithelial and transdermal delivery, as well as liposomal vesicles and nanoparticles. These continually advancing delivery systems enhance patient safety by reducing the dangers associated with drug administration and enhancing therapeutic results [17].

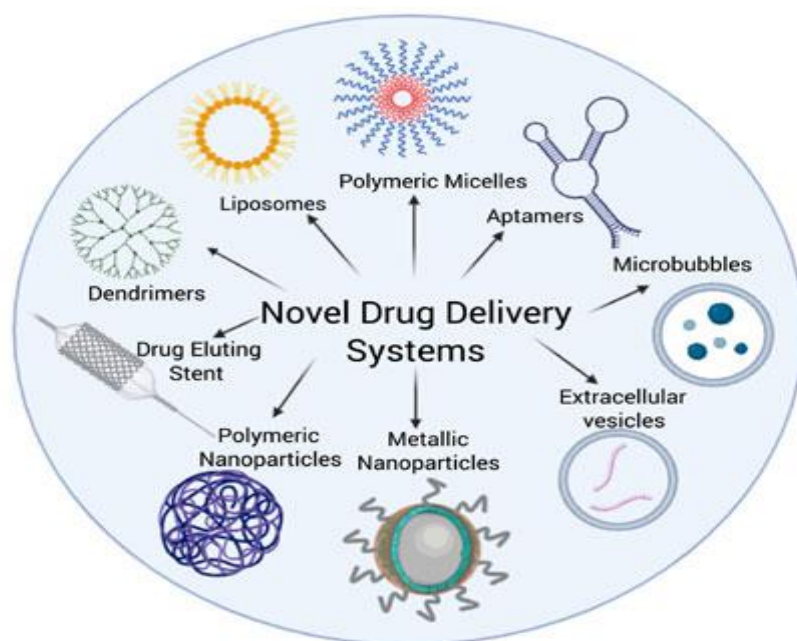


Figure 2: Types of Novel drug delivery systems

Characteristics of NDDS

- Enhance the bioavailability
- Facilitate regulated administration of medication
- Deliver the medicine unaltered to the target spot while circumventing healthy tissue.
- Stability and delivery must be preserved across several physiological factors.



e. Simple to administer, secure, and dependable.

f. Economically efficient [18].

The three primary objectives of NDDS

1. Ensure sustained drug release
2. Facilitate targeted administration to the site of action
3. Enhance patient compliance.

Nanoparticle Drug Delivery Systems not only diminish the frequency of administration but also mitigate peak and trough fluctuations, resulting in improved bioavailability [19].

Carrier based drug delivery systems

In pharmaceutical science, a carrier-based drug delivery system is a technology that uses specialized carriers to improve medication selectivity, efficacy, and safety. These carriers can enhance the solubility, stability, and transport of pharmaceuticals to specific sites, resulting in more effective therapeutic outcomes [20].

Liposomes, polymeric micelles, micro- and nanoparticles, and capsules are common examples of carrier systems. These transporters can encapsulate drugs and transport them to specific areas inside the body, allowing for controlled release and prolonged drug administration while maintaining the optimal blood concentration [21].

Micellar solutions, vesicle/liquid crystal dispersions, and nanoparticle dispersions, which are formed of tiny particles with diameters ranging from 10 to 400 nm, all have significant promises as colloidal carrier systems. The goal in developing these formulations is to construct systems with drug loading and release properties, a long shelf life, and low toxicity [22].

Carrier Based Drug Delivery System which are further classified as:

1. Nanoparticles,
2. Microspheres
3. Liposomes
4. Niosomes

1. Nanoparticles

Nanoparticles are dispersions or solid particles that range in size from 10 to 1000 nm. The drug is dissolved, entrapped, encapsulated, or bound to a nanoparticle matrix. Controlling particle size, features, and the release of pharmacologically active chemicals are the primary goals when designing nanoparticles as a delivery system to produce the medication's site-specific action at the therapeutically optimal rate and dosing regimen [23].

Classification of Nanoparticles According to Composition as presented in Figure 3 [24].

1. Metallic nanoparticles (Silver, Iron, Zinc, Copper)

Nanoparticles of metal oxides (TiO₂, ZnO, MoO₃)

Binary oxide nanoparticles (Bi₂O₃, CeO₂, CrO₂)

2. Carbon-Based Nanoparticles

Fullness Multi-Walled Carbon Nanotube (MWCNT)

Single-Walled Carbon Nanotube (SWCNT)

3. Dendrimers (Nanoscale nanoparticles)

4. Quantum dots (Cadmium Selenide, Caesium Telluride, Zinc Selenide, Zinc Sulphide)

5. Nanocomposites

Ceramic matrix nanoparticles (Al₂O₃, TiO₂, SiO₂)

Metal matrix nanoparticles (Co/Cr, Fe, Cr/Al₂O₃)

Polymer matrix nanoparticles (Polymer/TiO₂)

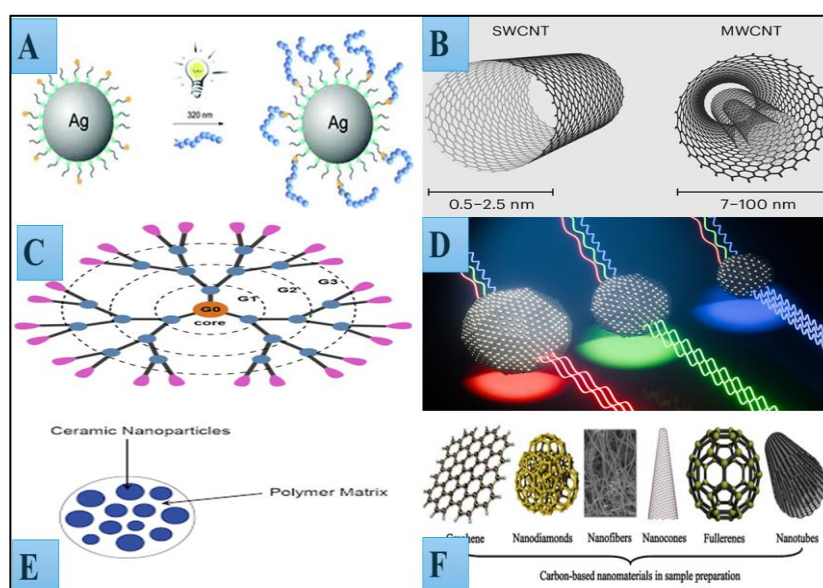


Figure 3: Classification of nanoparticles according to composition, Metallic nanoparticles (A), Carbon-Based Nanoparticles (B and F), Dendrimers (C), Quantum dots (D) and Nanocomposites (E).

2. Microspheres

These are usually microcapsules with spherical shapes, often ranging from 50 nm – 2 μm in size. Also known as microbeads, they are reported to contain a core substance; solid biodegradable microspheres with a medicine dispersed or dissolved throughout the particle-matrix may be used to deliver medications under regulated conditions as presented in Figure 4 [25].

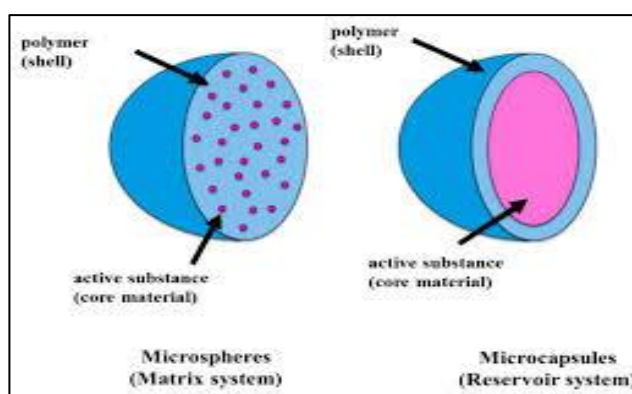


Figure 4: Structure of Microspheres

3. Liposomes

Liposomes were first identified in early 1965 by Alec D. Bangham, a term derived from the Greek words "lipo," meaning "fatty," and "soma," meaning "structure." Liposomes are diminutive, with diameters ranging from 50 nm to several micrometers [25].

Initially engaged in the study of in vitro simulated bio membrane behavior, they rapidly became esteemed as effective therapeutic instruments, especially for drug transport and targeted medicine. Liposomes are colloidal vesicular structures composed of phospholipid bilayers that entirely encase their hydrophilic core as presented in Figure 5 [26].

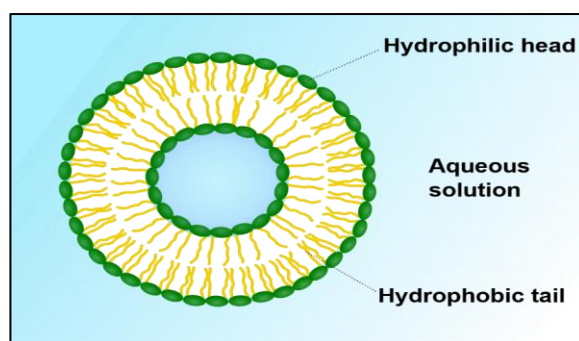


Figure 5: Structure of Liposomes

4. Niosomes

The non-ionic surfactant Span-60, which generates vesicles in niosomes, is frequently stabilized by the incorporation of cholesterol and a small quantity of an anionic surfactants such as diacetyl phosphate [27].

Niosomes and liposomes possess comparable capabilities in drug transport, demonstrating greater efficacy than free medicines [28].

Niosomes, while physically like liposomes in their bilayer composition, exhibit greater stability owing to the materials employed in their production. The subsequent two principal components employed in the preparation of Cholesterol and non-ionic surfactants as presented in Figure 6 [29].

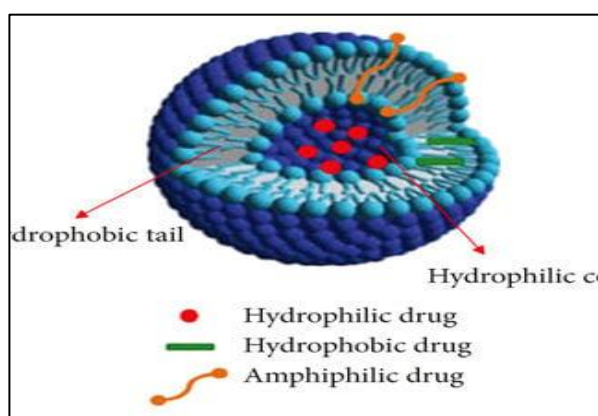


Figure 6: Structure of Niosome

Advantages of novel drug delivery systems

1. Pharmaceuticals provide protection against physical and chemical degradation.
2. Enhancing the distribution of tissue macrophages.
3. Mitigating adverse effects.



4. Amplifying pharmacological efficacy.
5. Prolonging drug release and reducing dosing frequency.
6. Facilitating direct drug delivery to the Central Nervous System.
7. Ensuring effective penetration.
8. Enhancing bioavailability.
9. Improving solubility.
10. Enabling targeted drug release [30].

Disadvantages of novel drug delivery systems

1. Immune responses may arise against intravenously given carrier systems.
2. Necessitates proficient personnel for production, warehousing, and management.
3. Necessitates advanced technology for the formulation of NDDS pharmaceuticals.
4. The disposal of gadgets or carriers may lead to environmental pollution.
5. There is a potential for dose dumping to occur.
6. Challenging to sustain the stability of dose formulations.
7. Certain modern drug delivery methods may be difficult to get in resource-limited or developing regions [31].

Approaches of novel drug delivery system

Novel Drug Delivery Systems (NDDS) embody sophisticated approaches that facilitate the accurate and efficient delivery of pharmaceuticals to target tissues, beyond traditional methods. They also seek to reduce drug degradation and loss, avert adverse side effects, and enhance bioavailability [32].

These methodologies can be categorized:

1. Targeted pharmaceutical delivery systems
2. Regulated pharmaceutical delivery systems
3. Stimuli-Responsive and Pulsatile Delivery Systems

Various types of drug carriers are now utilized, including soluble polymers, microparticles composed of natural or synthetic materials, and microcapsules. Biological carriers such as cells, cell ghosts, lipoproteins, liposomes, and micelles can also be utilized [33]. These carriers have significant flexibility; they can be engineered to decay gradually within the body or to respond to stimuli such as variations in pH or temperature. Crucially, they may be directed by conjugating antibodies to them, enabling the medicine to reach the precise location requiring treatment [34].

i. Targeted Drug Delivery Systems

Targeting refers to the capacity to steer the drug-loaded system to a specific site of interest or target tissue for therapeutic intervention. Three principal processes can be identified for targeting the specific areas of medication release [35]:

a. Passive Targeting

In passive targeting, chemotherapy drugs tend to accumulate specifically within solid tumors. This is due to the increased vascular permeability typically found in tumor tissue compared to healthy tissue as presented in Figure 7 and 8 [36].

b. Active Targeting

Active targeting is accomplished by altering the outside of drug carriers with ligands intended to attach to specific receptors on target cells. This method guarantees more targeted and accurate medication administration due to the great selectivity of ligand-receptor interactions as presented in Figure 7 and 8 [37].

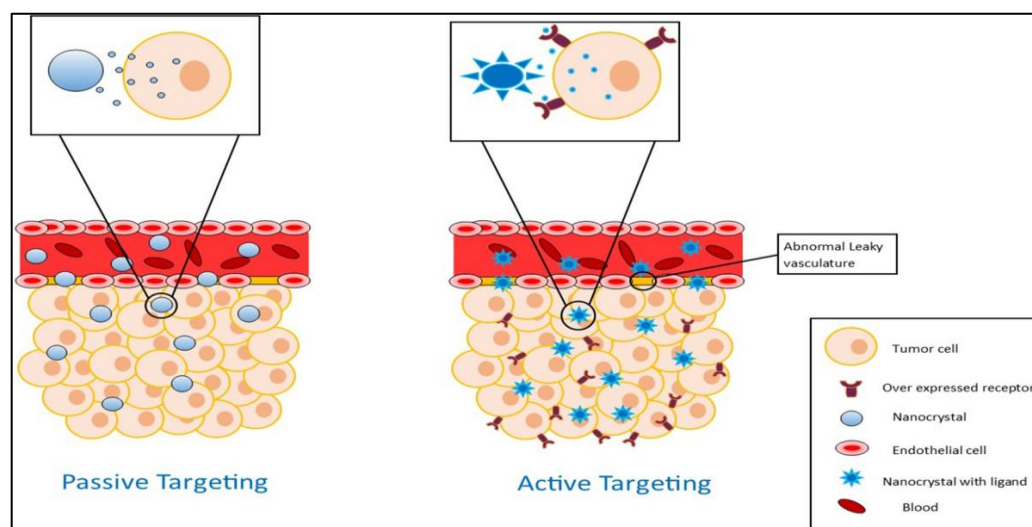


Figure 7: Mechanism of passive targeting and active targeting

c. Inverse Targeting

In Inverse Targeting, we want to prevent the reticuloendothelial system in the liver and spleen from sequestering the nanocarriers and eliminating them from the bloodstream as alien entities. To accomplish this, we deceive the RES by initially injecting alternative chemicals to occupy its attention. This enables the medicine to persist in the bloodstream for an extended duration and arrive at the target spot without the participation of the liver and spleen as presented in Figure 8 [38].

d. Ligand-mediated Targeting

In ligand-mediated targeting, ligands (such as antibodies, vitamins, or peptides) are affixed to the surface of the drug carrier. These ligands function by identifying receptors exclusively present on target cells, such as cancer cells. This method directs the medicine specifically to the diseased cells while sparing the healthy ones, hence minimizing adverse effects as presented in Figure 8 [26].

e. Physical Targeting

Physical targeting is a remarkable method for tumor localization. It is contingent upon alterations in the environment, like temperature, pH, or magnetic fields. These modifications provide precise control over the timing and location of the drug's release from the carrier as presented in Figure 8 [39].

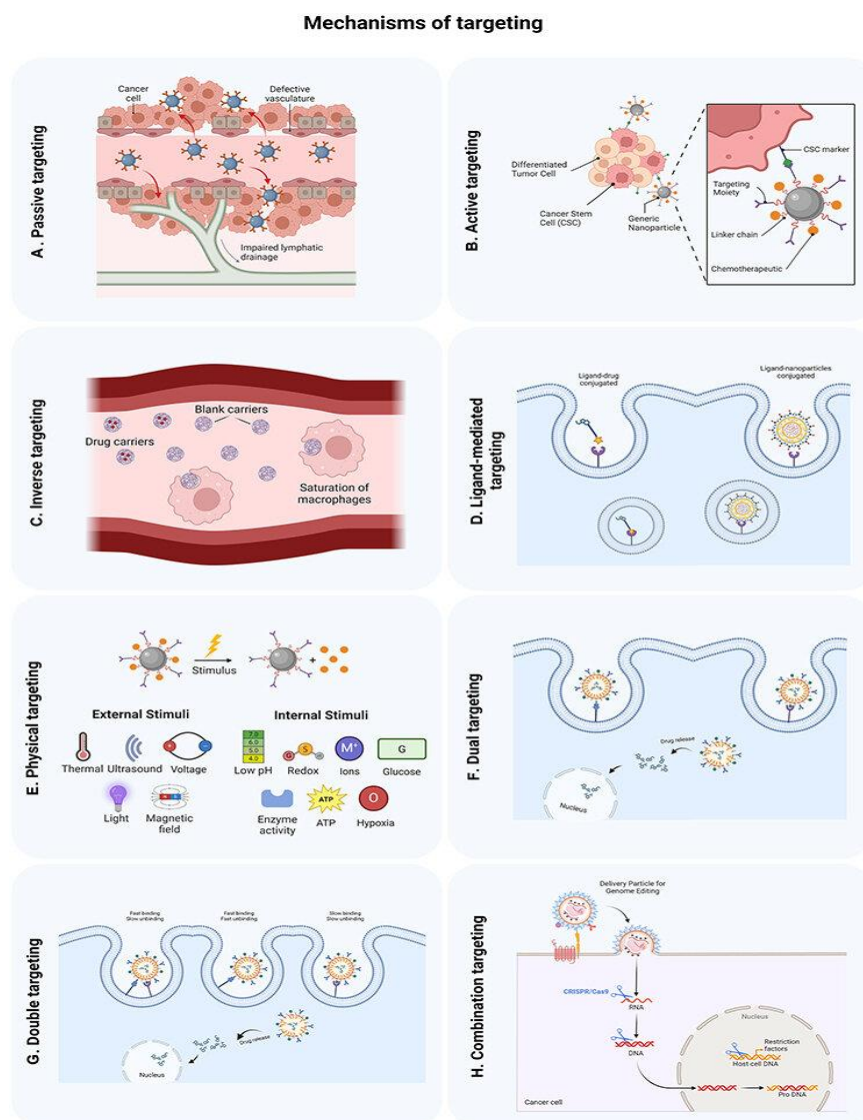


Figure 8: Different strategies of drug targeting. (A) Passive, (B) Active, (C) Inverse, (D) Ligand-mediated, and (E) Physical.

ii. Controlled Drug Delivery Systems

The drug release mechanism from its carrier - be it nano-, polymeric, or otherwise—is a pivotal determinant of medicinal efficacy or ineffectiveness. The major objective is to sustain consistent drug concentration in the bloodstream over prolonged durations, within the ideal therapeutic range [40].

This method enhances patient compliance by decreasing dosage frequency, while concurrently improving bioavailability and therapeutic effectiveness.

This is accomplished using five chemical or physical methods, or a combination thereof, to liberate the medication from the carriers [41]:

a. Desorption of Surface-Bound Drugs

This is the release of drug molecules that are only attached to the outer surface of the carrier. It happens as soon as the drug-loaded carrier touches body fluids due to changes in the surrounding environment. This mechanism depends on how strongly the drug is bound to the outer surface of the carrier as presented in Figure 9 [42].

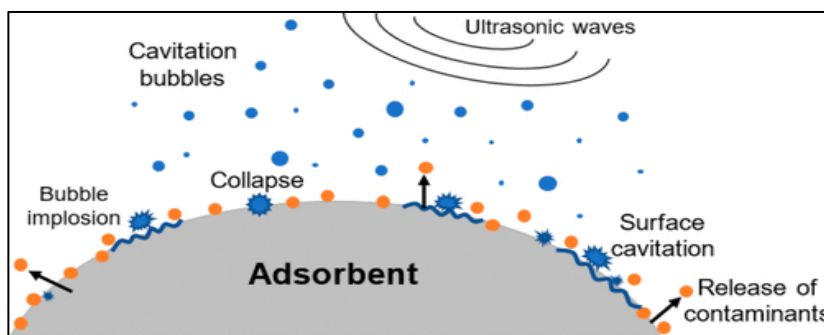


Figure 9: Structure of Desorption of Surface-Bound Drugs

b. Diffusion Through the Matrix

This occurs when the medication migrates from within the polymeric matrix to the exterior via minute pores, influenced by the concentration gradient. Due to the elevated drug concentration within the polymer, it will migrate toward the exterior medium (which has a lower concentration) through the diffusion property as presented in Figure 10 [43].

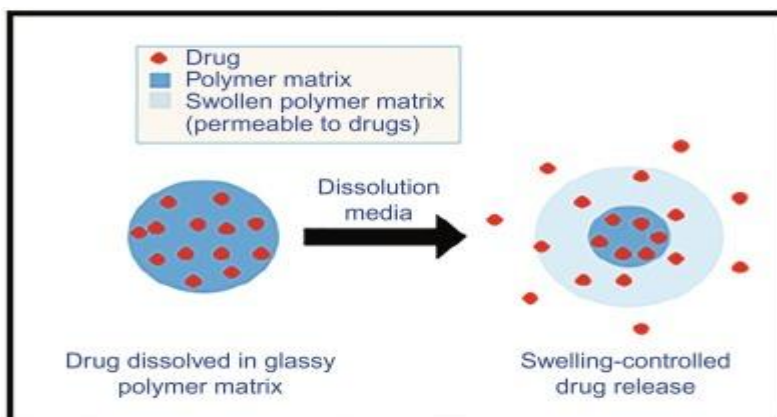


Figure 10: Diffusion Through the Matrix

c. Diffusion Through the Carrier Wall

In the case of nano capsules, the wall acts as a regulated barrier, where the drug is forced to penetrate the capsule wall to reach the outside. This depends on the permeability of the capsule shell as presented in Figure 11 [44].

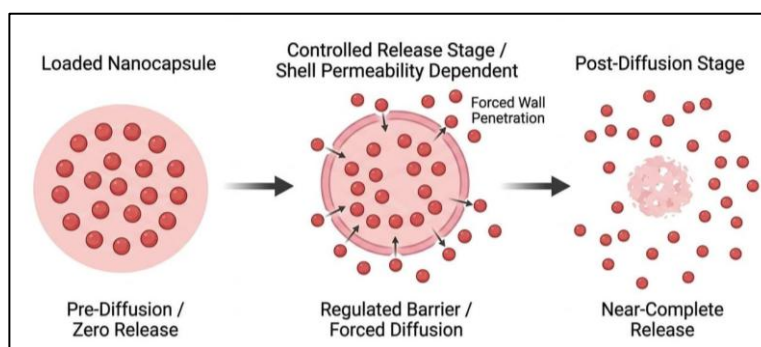


Figure 11: Diffusion Through the Carrier Wall

d. Carrier Matrix Erosion

In this technique, the medication does not await holes. The carrier progressively deteriorates or degrades, thereby releasing the encapsulated medicine within it as presented in Figure 12 [45].

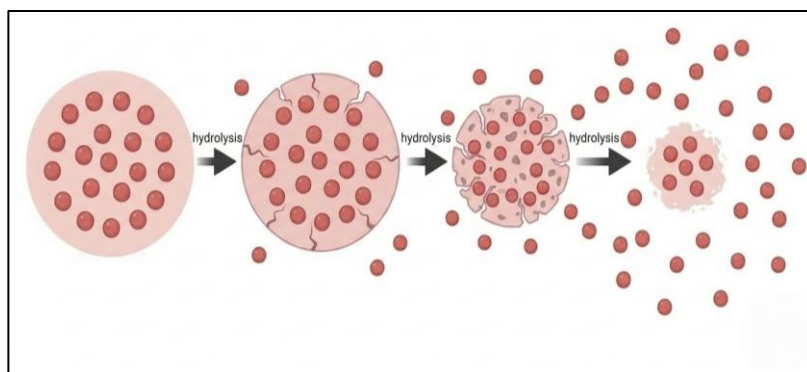


Figure 12: Carrier Matrix Erosion

e. Combined Erosion/Diffusion

This is a system that combines the erosion of the drug-loaded carrier with simultaneous drug diffusion as presented in Figure 13 [46].

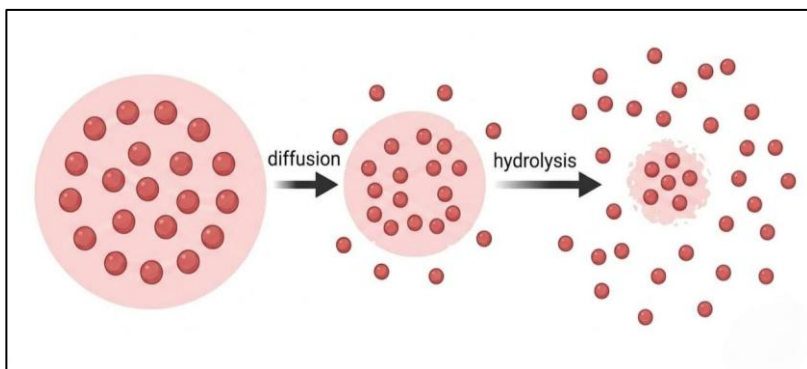


Figure13: Combined Erosion/Diffusion

iii. Stimuli-Responsive and Pulsatile Systems

This process involves the release of a drug from drug-encapsulating polymers in reaction to certain stimuli, like light, pH fluctuations, or temperature variations. This method precisely replicates the body's response: when blood glucose levels increase (a stimulus), insulin is secreted from the pancreas in reaction to this stimulus as presented in Figure 14 [47].

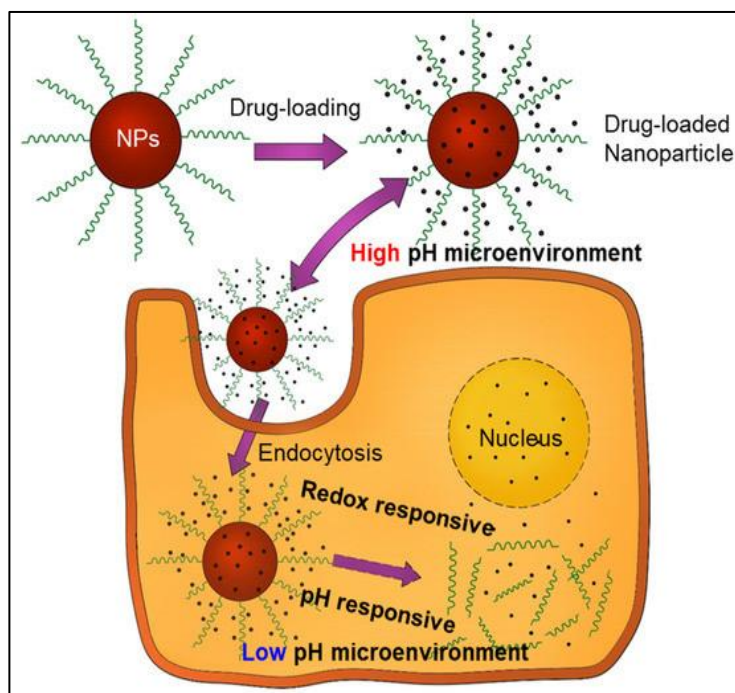


Figure 14: Stimuli-Responsive and Pulsatile Systems

Consequently, comprehending several methodologies for NDDS is crucial for enhancing the efficacy and safety of pharmaceuticals.

Applications of Novel Drug Delivery Systems

1. Targeted pharmacological delivery in oncological treatment.
2. Controlled and sustained drug release in the management of chronic conditions, including diabetes mellitus and cardiovascular disease.
3. Transdermal medication delivery methods.
4. Cellular and Gene Targeting Systems.
5. Advanced polymeric carriers that transport proteins and peptides
6. (biopharmaceuticals such as insulin) to specific organs while safeguarding these
7. substances from destruction.
8. Systems for pulmonary medication administration.
9. Targeted delivery methods for the brain and central nervous system [48].

Conclusion

Novel Drug Delivery Systems (NDDS) signify a significant progression in contemporary pharmaceutical science, offering efficient remedies to address the constraints of traditional dosage forms. These systems optimize therapeutic outcomes by administering medications at the correct dosage, timing, and target location, thereby improving bioavailability, decreasing drug degradation, and minimizing side effects. Recent breakthroughs in technologies, including nanoparticles, vesicular systems, and targeted drug delivery, have markedly enhanced the efficiency and control of drug release mechanisms.



The amalgamation of diverse disciplines such as pharmaceuticals, polymer science, molecular biology, and nanotechnology has expedited advancements in NDDS and broadened its applicability in treating numerous diseases, including cancer and neurological disorders. Notwithstanding these encouraging advancements, additional clinical trials and pharmacological assessments are necessary to ascertain their safety, efficacy, and successful implementation in clinical practice. In summary, NDDS possesses significant potential to advance pharmacotherapy and elevate patient quality of life in the future.

Conflict of interest: The authors declare that there is no conflict of interests.

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