

Drugs Design and Process Chemistry: A Factuality Study of Recent Advance in Drug Delivery Systems – A Comprehensive Review

Mohd. Wasiullah¹, Piyush Yadav², Shashikant Maury^{3,*}, Neha⁴

Abstract

Recent years have seen significant advances in drug design and process chemistry, mostly due to breakthroughs in drug delivery technologies. This study provides a thorough examination of current developments in drug delivery, emphasizing strategies that improve therapeutic efficacy, reduce adverse effects, and maximize pharmacokinetic profile. The effects of several strategies on drug stability, solubility, and bioavailability are examined, including controlled-release systems, targeted delivery methods, and nanoparticle-based delivery. This review also highlights the significance of green chemistry and sustainable practices while examining the function of process chemistry in scaling up drug manufacture to satisfy regulatory criteria. We analyze current trends, issues, and potential paths in the subject using a factual (flexible and factual) approach, offering a fundamental resource for scholars.

Keywords: Chemotherapy, tumor, nanoparticles, drug delivery, pharmacokinetic

INTRODUCTION

The field of drug design and process chemistry is integral to pharmaceutical research, focused on developing effective and efficient therapeutic agents. In recent years, innovations in drug delivery systems (DDS) have significantly influenced the design and manufacturing of drugs. Traditional drug delivery methods often fall short in terms of bioavailability, targeting specificity, and minimizing side effects. Addressing these limitations, novel drug delivery technologies now prioritize improving the pharmacokinetic and pharmacodynamic properties of therapeutics, aiming to enhance patient outcomes and treatment efficacy [1].

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This review delves into the factuality (flexible and factual) approach to drug delivery, bridging theoretical advancements with practical applications in process chemistry. By exploring recent innovations – such as nanoparticles, liposomes, and other targeted delivery methods – this study highlights how drug design and process chemistry intersect with advanced delivery systems to meet the demands of modern medicine. Additionally, this article examines the principles of green and sustainable chemistry in drug production, responding to the need for eco-friendly and economically viable manufacturing processes [2].

As DDS evolve, the pharmaceutical industry faces challenges in scaling up and maintaining the

quality of these complex systems while complying with regulatory standards. This review aims to provide a comprehensive understanding of the mechanisms, benefits, and limitations of emerging drug delivery technologies. By addressing the latest research, trends, and future directions, we aim to equip researchers and practitioners with insights into optimizing drug design, enhancing drug stability, and improving therapeutic outcomes through innovative delivery solutions. Pharmaceutical research, which aims to create effective and efficient medicinal agents, is heavily reliant on the fields of drug design and process chemistry. DDS advancements have had a big impact on drug design and production in recent years. Conventional drug delivery techniques frequently fail to minimize side effects, target specificity, and bioavailability. To improve patient outcomes and treatment efficacy, novel DDS increasingly place a higher priority on enhancing the pharmacokinetic and pharmacodynamic aspects of therapies [3].

To connect theoretical developments with real-world applications in process chemistry, this paper explores the factuality (flexible and factual) approach to drug delivery. By examining contemporary developments – like liposomes, nanoparticles, and other tailored delivery systems – this study demonstrates how process chemistry and drug design interact.

NANOCARRIER SYSTEMS

Nanocarrier systems have revolutionized drug delivery, offering promising strategies to improve bioavailability, targeting accuracy, and safety of therapeutics. These systems – designed at the nanoscale – are capable of transporting drugs directly to targeted cells or tissues, minimizing off-target effects and enhancing the therapeutic index of various treatments. Within the diverse range of nanocarrier systems, liposomes, nanoparticles, and micelles stand out due to their unique properties and broad applications, particularly in areas, such as cancer therapy, infectious diseases, and chronic conditions [4].

Liposomes are spherical vesicles composed of one or more phospholipid bilayers, closely resembling natural cell membranes. These bilayers allow liposomes to encapsulate both hydrophilic and hydrophobic drugs, protecting them from degradation in the bloodstream and allowing for controlled release. Liposomes can be surface modified with ligands or antibodies for active targeting, making them highly adaptable for a range of therapeutic purposes. Their biocompatibility and low toxicity have led to their successful incorporation in FDA-approved drug formulations, particularly in cancer treatment and antimicrobial therapy [5].

Nanoparticles, often classified by their composition (e.g., polymeric, lipid, or metal-based), offer versatile platforms for drug delivery. Polymeric nanoparticles, for instance, allow precise control over drug release rates, while lipid-based nanoparticles enhance the solubility of poorly water-soluble drugs. Nanoparticles can also be engineered to respond to specific environmental triggers (e.g., pH, temperature) at the target site, enabling on-demand drug release. Their small size and surface-modifiable properties allow.

Nanoparticles to accumulate in specific tissues or cross biological barriers, such as the blood-brain barrier, widening their application in challenging therapeutic areas.

Micelles are colloidal carriers formed by the self-assembly of amphiphilic molecules in aqueous solutions. Due to their hydrophobic core and hydrophilic shell, micelles are especially suitable for delivering hydrophobic drugs, which are otherwise challenging to administer. Micelles can enhance drug solubility, reduce drug precipitation, and improve circulation times, making them ideal for conditions requiring prolonged release [6]. Like liposomes and nanoparticles, micelles can be modified with targeting ligands to increase specificity and reduce systemic side effects.

Drug delivery has been transformed by nanocarrier systems, which provide promising methods to increase treatments' bioavailability, precision of targeting, and safety. These nanoscale-designed

devices can deliver medications straight to specific cells or tissues, reducing side effects and raising the therapeutic index of different therapies. Liposomes, nanoparticles, and micelles are notable among the wide variety of nanocarrier systems because of their special qualities and wide range of uses, especially in fields like cancer treatment, infectious disorders, and chronic illnesses [7].

Liposomes are spherical vesicles that closely resemble natural cell membranes and are made up of one or more phospholipid bilayers. Both hydrophilic and hydrophobic medications can be encapsulated in liposomes thanks to these bilayers, which prevent bloodstream breakdown and enable controlled release. Ligands or antibodies can be used to alter the surface of liposomes [8].

Liposome

Liposomes are spherical vesicles that closely resemble natural cell membranes and are made up of one or more phospholipid bilayers. Both hydrophilic and hydrophobic medications can be encapsulated in liposomes thanks to these bilayers, which prevent bloodstream breakdown and enable controlled release. Liposomes are very versatile for a variety of therapeutic applications since their surface can be altered with ligands or antibodies for active targeting. They have been successfully included into FDA-approved therapeutic formulations due to their low toxicity and biocompatibility, especially in antimicrobial therapy and cancer treatment [9, 10].

Nanoparticles

Nanoparticles provide flexible drug delivery platforms and are frequently categorized by their composition (e.g., polymeric, lipid, or metal-based). For example, lipid-based nanoparticles improve the solubility of medications that are poorly soluble in water, while polymeric nanoparticles provide precise control over drug release rates. On-demand medication is made possible by the ability to design nanoparticles to react to environmental cues (such as pH or temperature) at the target location. Nanoparticles can aggregate tissues or pass across biological barriers, like the blood-brain barrier, because of their small size and surface-modifiable characteristics, which expands their use in difficult therapeutic areas [11].

Micelles

Micelles are colloidal carriers created when amphiphilic molecules in aqueous solutions self-assembled. Micelles are particularly well-suited for delivering hydrophobic medications, which are otherwise difficult to give, because of their hydrophilic exterior and hydrophobic center. Micelles are perfect for circumstances needing longer release because they can improve circulation times, decrease drug precipitation, and increase drug solubility. Micelles can be altered by targeting ligands to improve specificity and lessen systemic side effects, just like liposomes and nanoparticles [12].

In conclusion, three of the most common forms of nanocarriers in DDS are liposomes, polymeric nanoparticles, and micelles. They are vital in modern medicine because of their adaptability, ability to target specific areas, and capacity for controlled drug release, especially in areas where accurate, controlled, and focused drug delivery is crucial.

TARGETED DDS

A drug delivery method that targets tissues or cells is known as a targeted DDS (TDDS) (Figure 1). By delivering medications to target tissues or cells via a range of different routes, including oral administration, intravenous injection, skin patches, etc., this drug system can increase the effectiveness of the medication while lowering its negative effects on healthy tissue [13]. It can do this by using microparticles, nanoparticles, nanotechnology, liposomes, polymers, or other carriers. In contrast to conventional DDS, which rely on drug absorption through biofilms, they achieve site-specific release of the medication from the dosage form.

By delivering therapeutic compounds straight to cells or tissues, TDDS increase treatment effectiveness while lowering negative effects. This method differs from conventional drug

administration, which involves distributing medications throughout the body, frequently affecting both healthy and diseased cells. Drugs are enclosed in carriers (such liposomes, nanoparticles, or micelles) and released selectively at the site of interest in targeted drug delivery. The two primary methods for achieving this targeting are active targeting and passive targeting [14].

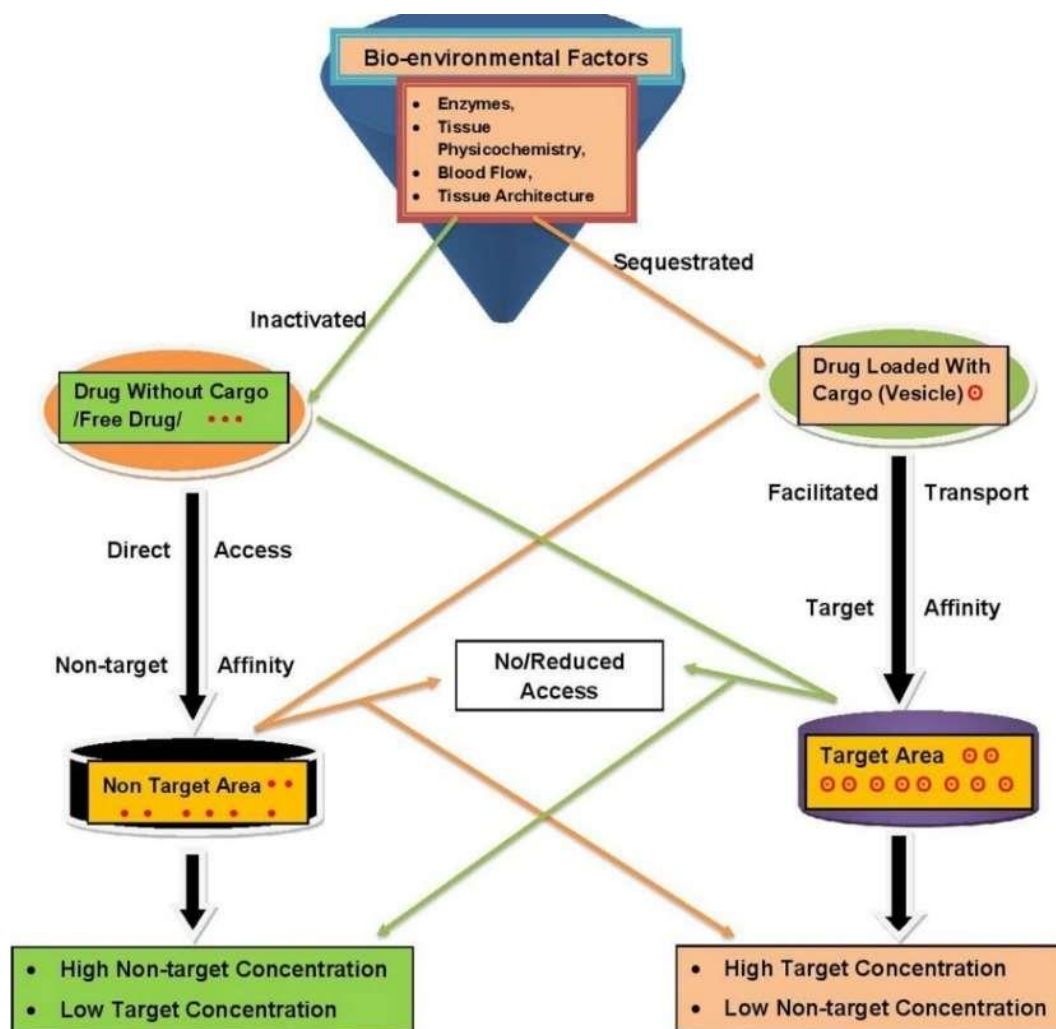


Figure 1. Drug targeting principles.

Active Targeting

Adding ligands or molecules to the drug carrier that selectively attach to receptors or biomarkers on target cells is known as active targeting. These ligands could be sugars, peptides, antibodies, or other substances that identify and attach to target cell surface receptors. For instance, a lot of cancer cells overexpress specific receptors, such folate receptors, which folate-modified drug carriers can target. More accurate and regulated drug distribution is made possible once the drug carrier is bound and absorbed by the target cell. When targeting cell types in a mixed cellular environment, active targeting is especially beneficial since it increases selectivity and reduces off-target effects [15].

Passive Targeting

The natural distribution and buildup of drug carriers in particular tissues, frequently because of the target area's distinct physiological features, is the foundation of passive targeting. A fundamental idea in passive targeting, the enhanced permeability and retention (EPR) effect is especially pertinent to cancer treatment. In contrast to normal tissues, tumor tissues often have extensive holes and leaky blood arteries, which facilitate the accumulation of drug carriers and nanoparticles. It is very useful

for delivering anticancer drugs because of its passive accumulation, which raises drug concentration at the tumor location. Passive targeting's reliance on biological variables, which can differ between patients and circumstances [16].

Control Release DDS

To increase treatment effectiveness and reduce side effects, controlled-release DDS are made to release therapeutic substances over a longer period at a predefined rate. Controlled-release systems maintain constant, therapeutic concentrations of the drug, lowering the frequency of doses and improving patient compliance in contrast to traditional drug delivery, which frequently leads to rapid release and fluctuating drug levels. Hydrogels and polymer-based technologies stand out among the other controlled-release techniques.

Hydrogel-Based System

Hydrogels are three-dimensional networks of hydrophilic polymers that are perfect for controlled medication release because they can absorb enormous volumes of biological fluids or water. As the hydrogel expands or breaks down, these networks can encapsulate medications inside their structure for progressive release. By modifying the cross-linking density, polymer composition, and environmental triggers (e.g., pH, temperature, or enzymes), drug release from hydrogels can be regulated. Because of their excellent biocompatibility and ability to replicate the extracellular matrix, hydrogels can be used in tissue engineering, wound healing, and localized medication delivery [17].

Polymers-Based System

Drugs are encapsulated or embedded in a matrix or coating using synthetic or natural polymers in polymer-based controlled-release systems. The medication is released at a regulated pace as the polymer dissolves, erodes, or degrades. Drug release can be precisely regulated to satisfy therapeutic needs by altering the polymer's composition, molecular weight, and rate of degradation. Polylactic acid (PLA), polyglycolic acid (PGA), and poly (lactic-co-glycolic acid) (PLGA) are examples of biodegradable polymers that are frequently employed for this purpose since they spontaneously decompose in the body and do not require surgical removal once the medicine is entirely delivered. Systems based on polymers are used extensively in fields, such as hormone distribution, cancer treatments, and postoperative. Scientists at Integral Biosystems are skilled at identifying the ideal circumstances for parenteral drug delivery by carrying out the appropriate testing for the route. Our goal is to develop injectable medicine formulations that are as high-quality and high-performing as possible [18].

INJECTABLE DDS

Isotonicity, biocompatibility with physiological fluids and tissues, and drug solubility in physiological fluids are essential components for injectable formulations, even though each drug delivery route has elements to consider when designing an efficient delivery system (Figure 2).

Because drug precipitation after injection can result in venous irritation, phlebitis, hemolysis, and hepatotoxicity, the medication's solubility at pH 7.4 in physiological fluids is crucial for intravenous formulations. Because they transform into a non-ionized state at pH 7 and above, drugs with a pka of less than pH 6 are more likely to precipitate [19].

By avoiding the digestive system and increasing bioavailability, injectable DDS offer a quick and effective method of delivering therapeutic substances straight into the body. Treatments requiring precise dosage, quick onset, or the delivery of chemicals that are unstable or poorly absorbed orally benefit greatly from injectable methods. Depot injections and biologics delivery systems are notable among injectable methods due to their capacity to provide targeted, regulated, and prolonged drug release.

Parenteral Route of Drug Administration

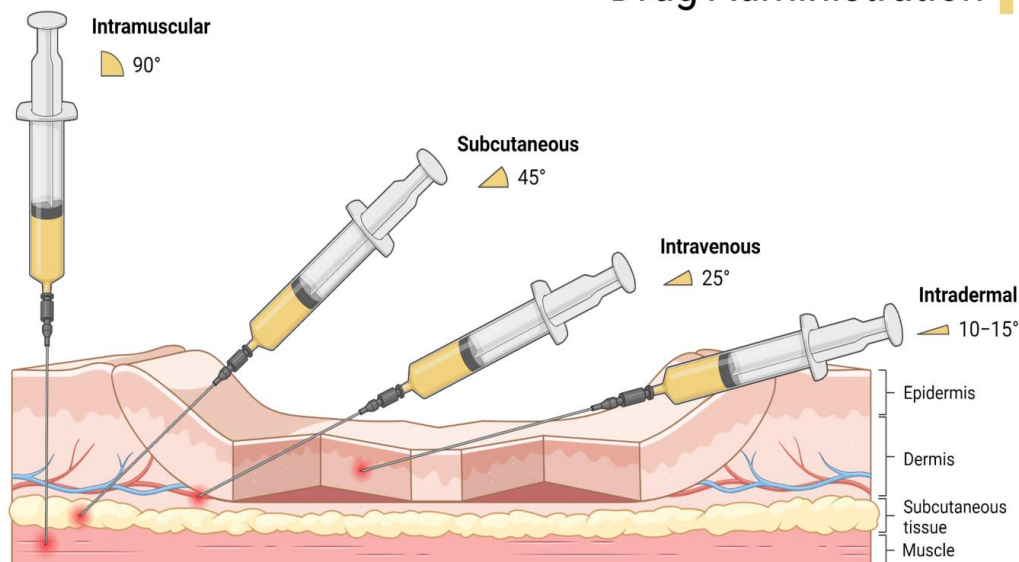


Figure 2. Examples of injectable routes.

Depot Injection

Depot injections are a kind of long-acting injectable drug delivery technique that allows the drug to be progressively released into the bloodstream over a lengthy period by forming a “depot” or reservoir at the injection site. Depot formulations are usually created with oil-based solutions or biodegradable polymers that release the medication as they dissolve or break down gradually. Because it reduces the need for frequent dosage, this method is especially advantageous for long-term problems like hormone replacement, mental health issues, and some infectious infections. Depot injections increase patient adherence and assist in preserving consistent therapeutic medication levels, minimizing variations that may result in adverse effects or diminished effectiveness [20].

Biologics Delivery

To stay stable and effective, biologics – such as gene treatments, vaccines, and monoclonal antibodies – often need to be handled and delivered carefully. Since many biologics degrade in the digestive tract, injectable administration is the main way to administer them. Enhancing stability, bioavailability, and accuracy in targeting cells or tissues are the main goals of developments in injectable biologics systems. Specialized injectable formulations, like liposomes or nanoparticle carriers, can enhance the distribution of these big, delicate molecules to their intended locations while preventing deterioration. Biologics is frequently administered by subcutaneous, intravenous, and intramuscular methods; formulations and delivery systems are frequently tailored to the size, solubility, and desired release profile of the molecule [21].

ORAL DRUG DELIVERY

The most popular and practical method of delivering therapeutic agents is still oral drug delivery, which promotes patient compliance and convenience of usage. However, there are drawbacks to oral distribution, including poor absorption, low bioavailability for certain medications, and breakdown in the stomach’s acidic environment. To get over these obstacles, novel formulations have been created, such as enteric coatings and nanocrystals, which increase the effectiveness and dependability of oral medication delivery.

Nanocrystals Formulation

Sub-micron-sized medication particles known as nanocrystals are stabilized by polymers or surfactants to improve solubility and bioavailability. Due to their low water solubility, many medications have restricted absorption and, as a result, are less effective when taken orally. This is addressed by nanocrystal technology, which increases the drug's surface area and rate of dissolution in gastrointestinal fluids by decreasing particle size. This enables more effective bloodstream absorption, which makes nanocrystals especially helpful for medications with limited bioavailability or poor water solubility. Formulations containing nanocrystals have been effective in treating diseases, such as cancer, heart disease, and problems of the central nervous system [22].

Enteric Coating

A polymer-based barrier called enteric coating is used on oral drugs to prevent stomach acid from breaking them down. This coating is made to withstand the stomach's acidic environment and only dissolve in the intestines' higher pH environment, which allows for drug absorption without running the risk of acid-induced destruction. Acid-sensitive medications like proton pump inhibitors, some antibiotics, and certain vitamins are frequently coated with enteric. They also help with targeted distribution to the intestines, which is helpful when localized therapeutic action is required, such as in inflammatory bowel.

TRANSDERMAL DDS

By delivering a regulated and sustained release of medication straight into the systemic circulation, transdermal drug delivery devices (TDDS) provide a simple and non-invasive method of drug administration through the skin. Transdermal administration methods circumvent first-pass metabolism via the liver and gastrointestinal tract, which frequently results in increased bioavailability when compared to oral or injectable delivery methods. They are extensively utilized for a variety of pharmaceuticals, such as hormone treatments, painkillers, and cardiovascular medications. Innovative techniques, like microneedles and nanoparticles, have been developed to get beyond the skin's natural barrier qualities and increase the efficacy of transdermal drug [23].

Microneedle

Drugs that might otherwise find it difficult to get beyond the skin's barrier can be delivered via microneedle systems, which use tiny, minimally invasive needles to gently penetrate the stratum corneum, the skin's outermost layer. Because microneedles are small enough to avoid touching pain receptors, the administration is essentially painless. These devices, which can be made of solid or dissolvable microneedles, are frequently employed to administer small molecule medications, peptides, or vaccinations. Drugs can diffuse into the skin or deeper layers thanks to the microchannels the microneedles produce, providing precise and long-lasting drug release. Because of their ease of use, microneedle patches are perfect for self-administration and increasing patient [24].

Nanoparticles for Transdermal Drug

In transdermal applications, nanoparticles can act as carriers to help drugs pass through the epidermis' outer layer and increase the bioavailability of active substances. Nanoparticles can interact with the skin's surface and improve drug penetration because of their small size and large area. Transdermal formulations frequently contain liposomes, polymeric nanoparticles, and solid lipid nanoparticles. Encapsulating hydrophobic or hydrophilic medications, these nanoparticles offer controlled and prolonged release while shielding delicate medications from deterioration. Transdermal systems based on nanoparticles are especially useful for cosmetic applications and for the delivery of medications, such as hormones, antioxidants, and anti-inflammatory

FUTURE DIRECTION

With a focus on enhancing accuracy, effectiveness, and patient compliance, ongoing developments in materials science, biotechnology, and nanotechnology are influencing the direction of DDS. These developments are improving the bioavailability of hard-to-deliver medications, decreasing side

effects, and enabling more individualized and focused therapies. The following are some crucial areas for future medication delivery research:

Precision and Customized Medicine

DDS are being developed to customize therapy according to lifestyle, environmental, and genetic factors as we progress toward more tailored treatments. Individual patient-specific therapy will be possible with the combination of DDS and pharmacogenomics. For instance, depending on a patient's genetic profile, customized drug delivery devices may target molecular markers or modify the rates at which drugs are released. This will lessen side effects, increase treatment effectiveness, and enable improved real-time drug performance monitoring.

Intelligent Medication Administration System

Smart drug delivery systems (SDDS) provide controlled, site-specific, and on-demand medication release by adapting dynamically to physiological variables or external stimuli. These devices may have "sensors" that pick up on environmental indicators (such as pH, temperature, or enzymes) and deliver the medication only when required. In chronic illnesses, where medications must be given only when specific biomarkers or disease signs are present, this could be particularly helpful. These intelligent systems can lower the chance of overdosing or underdosing and provide more accurate therapy.

Nanotechnology and Nano Medicine

Drug delivery is about to undergo a revolution thanks to nanotechnology, which makes it possible to create more compact and effective carriers that can deliver medications straight to the intended location. Drug stability, solubility, and targeted administration are being improved via the engineering of nanocarriers, such as dendrimers, liposomes, and nanoparticles. Additionally, nanomedicines can minimize harm to healthy tissues while delivering treatments that are difficult to treat, like biologics, genetic therapies, and anticancer agents. In the future, neurological disorders might be treated with even more functionalized, smaller nanoparticles that can pass through biological barriers like the blood-brain barrier [25].

Personalized and Targeted Drug Administration

The objective is to minimize harm to healthy tissues while delivering medications straight to the site of action, such as cancer cells. Personalized medicine delivery is becoming a reality thanks to developments in biomarker-based targeting.

For accurate drug delivery, especially in cancer treatment, antibody-drug conjugates and other ligand-receptor targeted systems are being utilized more and more.

CONCLUSIONS

In conclusion, by overcoming the drawbacks of conventional medicines, current developments in DDS have the potential to completely transform the way that many diseases are treated. More accuracy, effectiveness, and safety in drug administration are the focus of these developments, with significant breakthroughs including.

Nanotechnology

By removing obstacles, like the blood-brain barrier and enabling targeted medication administration, nanoparticles and nanocarriers improve therapeutic results.

Personalized Medicine

It is increasingly possible to customize medication distribution according to each patient's unique genetic, metabolic, and illness profiles, increasing specificity and lowering adverse effects.

Gene and RNA-based Therapies

New avenues for treating cancer and genetic problems are being made possible by the development of mechanisms for delivering genetic material, such as mRNA and RNAi.

Biodegradable Materials

To reduce toxicity and provide more environmentally friendly and biocompatible solutions, biodegradable polymers are being used more and more.

Long Acting and Controlled Release

Over time, patient compliance and treatment efficacy are enhanced by formulations that offer prolonged, controlled medication release.

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