WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 15, 1185-1211. Review Article ISSN 2277–7105

REVIEW THE LATEST DEVELOPMENTS IN THE DRUG DELIVERY SYSTEM INCLUDING THE NANOPARTICLES AND THEIR APPLICATION IN IMPROVING DRUG BIOAVAILABILITY AND PATIENT COMPLIANCE

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Article Received on
21 June 2024,

Revised on 11 July 2024,
Accepted on 31 July 2024

DOI: 10.20959/wjpr202415-32998

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ABSTRACT

Nanoparticle-based drug delivery systems have emerged as a promising approach to address the limitations of conventional drug formulations, particularly in terms of improving drug bioavailability and enhancing patient compliance. This abstract reviews the latest developments in nanoparticle technology and its applications in pharmaceutical research and development. Recent advancements in nanoparticle formulations, including liposomes, polymeric nanoparticles, dendrimers, and solid lipid nanoparticles, have facilitated the encapsulation of drugs, protecting them from degradation and enabling controlled release. These formulations have demonstrated the ability to enhance drug solubility and stability, leading to improved bioavailability and therapeutic efficacy. Targeted drug delivery using functionalized nanoparticles has gained significant attention for its potential to selectively deliver drugs to specific tissues or cells, minimizing systemic side effects and maximizing therapeutic outcomes. Stimuli-responsive nanoparticles, capable of releasing drugs in response to environmental cues, offer precise control over drug release kinetics, paving the way for personalized medicine approaches. Moreover, nanoparticle-based drug delivery systems have shown promise in improving patient compliance by offering convenient dosing regimens and reducing the frequency of drug administration. Long-acting nanoparticle formulations have the potential to enhance adherence to treatment regimens and optimize therapeutic outcomes, particularly for chronic conditions.

KEYWORDS: Nanoparticle formulation, Improved drug bioavailability, Targeted drug delivery, Control Release system, improved patient compliance.

INTRODUCTION

Delivering Medicine at controlled rate, slow delivery, targeted Delivery are other veritably seductive styles and have been pursued roundly. Despite several advantages, pharmaceutical companies are reluctant to invest more in natural product- grounded medicine discovery and medicine delivery systems.[1] Nanomaterials can be well- defined as a material with sizes ranged between 1 and 100 nm, which the borders of Nano drug starting from biosensors, microfluidics, medicine delivery, and microarray tests to towel engineering.[2-3] The conventional optical lozenge forms are eye drops, eye dormancies, eye Gels, eye vexation results, eye results, eye ointments, eye injections, sol to gel systems[4] Bringing a new medicine through discovery, clinical testing, development, and nonsupervisory blessing is presently estimated to take a decade and cost well over$ 120 million. New medicine delivery systems may regard for as important as 40 of US retailed medicine products by 2000.[5-6] On one hand, the design of nanomaterials as medicine carriers should address the following crucial issues (i) sufficient biocompatibility and biodegradability; (ii) good stability in physiological conditions; and (iii) high medicine lading capacity and low toxin. On the other hand, besides the primary demand for safety and remedial efficacy, artificial scale- up for DDSs is also a prerequisite for this type of new nanomaterials in clinical operations as shown. To date, a myriad of accoutrements, similar as polymers, Lipids and inorganic accoutrements, has been developed And served as medicine carriers to control the release of loads[7-8], These elaborately designed smart or stimulants- responsive Nano platforms can respond to endogenous and/ or exogenous encouragement as shown in Figure 1. The endogenous triggers similar as pH variations, hormone position, enzyme attention, smallbio-molecules, glucose or redox grade[9-10], Redox responsive stimulants have gained great attention for complaint remedy and extensively used in intracellular DDSs.[11-12] The redox eventuality in microenvironments is multivariate in different apkins, which can be exploited to design redox-sensitive delivery systems. The design and fabrication of nanoparticles responsive to Glutathione (GSH) can be a promising approach for targeting medicine delivery.[13] The GSH reduction is a well- known redox system within cancer cells. On one hand, attention of GSH in blood and normal extracellular matrices are reported to be 2- 20 μM, at the same time GSH situations within cancer cell rangesfrom 2 to 10 mM, which is 100- to 500- fold advanced than the normal ranges.[14] In recent times, biodegradable polymeric Nanoparticles have

attracted considerable attention as implicit medicine delivery bias in view Of their operations in the controlled release of medicines, in targeting particular organs apkins, As carriers of DNA in gene remedy, and in their capability to deliver proteins, peptides and genes Through the paroral route. A Novel Drug Delivery System (NDDS) can be defined as a new approach That combines innovative development, phrasings, new technologies, new Methodologies for delivering pharmaceutical composites in the body as demanded to safely Achieve its asked pharmacological goods. Characteristics of Novel Drug Delivery System Increase the bioavailability give controlled delivery of medicine Transport the medicine complete to the point of action avoiding then on-diseased towel. Stable and delivery be maintained under colorful physiological variables. Easy to administer, safe and dependable. Cost-effective.3.[15]

Characteristics of Novel Drug Delivery System

- Increase the bioavailability
- Provide controlled delivery of drug
- Transport the drug intact to the site of action avoiding the non-diseased tissue.
- Stable and delivery be maintained under various physiological variables.
- Easy to administer, safe and reliable.[16]

COMPONENT OF NANOCAPSULE

- Core Material
- Shell Material
- Surface Modifications
- Stabilizers and Emulsifiers
- Solvents and Carriers
- Crosslinking Agents
- Biodegradable Materials
- Modifiers for Control Release

METHOD OF PREPARATION OF NANOCAPSULE

- Emulsification –Solvent Evaporation Method
- Nanoemulsion Templating Method
- Solvent Displacement Method
- Supercritical Fluid Technology
- Coacervation Method
- Layer-by-Layer (LbL) Assembly

- Nano-precipitation
- Emulsification-conservation
- Phase inversion
- Double emulsification

Drug delivery systems can be classified based on various criteria, including the route of administration, release mechanism, and the carrier used. Here is a broad classification of drug delivery systems:

Based on Route of Administration

Oral Drug Delivery: Tablets, capsules, syrups, etc.

Parenteral Drug Delivery: Intravenous, intramuscular, subcutaneous, etc.

Topical Drug Delivery: Creams, ointments, patches, etc.

Pulmonary Drug Delivery: Inhalers, nebulizers, etc.

Transdermal Drug Delivery: Patches, gels, etc.

Based on Release Mechanism

Immediate Release Systems: Release the drug rapidly after administration.

Release Systems: Slow and controlled release of the drug over an extended period.

Sustained Release Systems: Maintains therapeutic levels of drug in the bloodstream for an extended duration.

Pulsatile Release Systems: Mimics natural body rhythms by releasing the drug in pulses.

Targeted Release Systems: Releases the drug specifically at the site of action.

Based on Carrier System

Polymeric Drug Delivery: Using polymers to control drug release.

Lipid-Based Drug Delivery: Liposomes, micelles, and lipid nanoparticles for drug encapsulation.

Nanoparticle-Based Drug Delivery: Utilizing nanoscale carriers for drug delivery, including liposomes, micelles, and nanoparticles.

Polymeric Microparticle-Based Drug Delivery: Microspheres and microcapsules for controlled drug release.

Dendrimer-Based Drug Delivery: Using dendrimers as drug carriers.

Based on Nature of Drug

Conventional Drug Delivery: Simple drug formulations without specialized delivery systems.

Biological Drug Delivery: Delivery systems for biologics such as proteins, peptides, and nucleic acids.

Based on Technology Used

Microsphere Technology: Using microspheres for controlled drug release.

Nanotechnology-Based Delivery: Involving nanoscale materials for drug delivery.

Implantable Drug Delivery: Devices implanted under the skin for controlled drug release.(24)

Based on Application

Cancer Drug Delivery: Targeted drug delivery for cancer treatment.

Gene Delivery Systems: Systems designed for the delivery of genetic material.

Based on Release Trigger:

Stimuli-Responsive Drug Delivery: Releasing drugs in response to specific stimuli like pH, temperature, or enzymes.

Programmable Drug Delivery: Allowing for customizable drug release schedules.

These classifications highlight the diverse range of drug delivery systems developed to optimize therapeutic outcomes, minimize side effects, and enhance patient compliance. Keep in mind that the field is continually evolving, and new categories and technologies may emerge as research progresses.

Nanotechnology encompasses a broad range of techniques and applications at the nanoscale, typically dealing with structures or materials with dimensions between 1 and 100 nanometers. In the context of drug delivery and bioavailability enhancement, several types of nanotechnology are commonly employed. Here are some key types.[25]

Nanoparticles

Liposomes: Spherical vesicles composed of lipid bilayers. Liposomes can encapsulate both hydrophilic and hydrophobic drugs, improving drug solubility and bioavailability.

Polymeric Nanoparticles: Particles made from biodegradable polymers that can encapsulate drugs and release them in a controlled manner, enhancing drug stability and delivery.

Metal and Metal Oxide Nanoparticles: Materials like gold, silver, or iron oxide nanoparticles can be used for drug delivery, imaging, and therapeutic purposes.[26]

Nanocapsules

Polymeric Nanocapsules: Hollow structures composed of a polymeric shell that can encapsulate drugs. They provide controlled release and protection of the drug payload.

Dendrimers: Highly branched, tree-like structures with a well-defined architecture. Dendrimers can carry drugs on their surface or within their structure, offering precise control over drug release.[55]

Nanoemulsions: Stable, colloidal dispersions of oil droplets in water. Nanoemulsions can improve the solubility of lipophilic drugs and enhance their absorption.

Carbon Nanotubes: Cylindrical structures made of carbon atoms. Carbon nanotubes can be functionalized to carry drugs and targeted to specific cells or tissues.

Nanogels: Hydrogel nanoparticles that can encapsulate drugs. Nanogels provide a three-dimensional network for drug delivery, offering controlled release and improved stability.[56]

Nanofibers: Fibrous structures with diameters in the nanometer range. Nanofibers can be used as drug delivery scaffolds, providing a large surface area for drug release.

Nanostructured Lipid Carriers (NLCs): Lipid-based nanoparticles with a structured lipid matrix. NLCs can improve drug loading capacity and stability, enhancing drug delivery efficiency.

Quantum Dots: Semiconductor nanocrystals with unique optical properties. Quantum dots can be used for imaging and diagnostic purposes in addition to drug delivery.

Nanoporous Materials: Materials withanoscale pores that can be used for controlled drug release. Examples include mesoporous silica nanoparticles.[57]

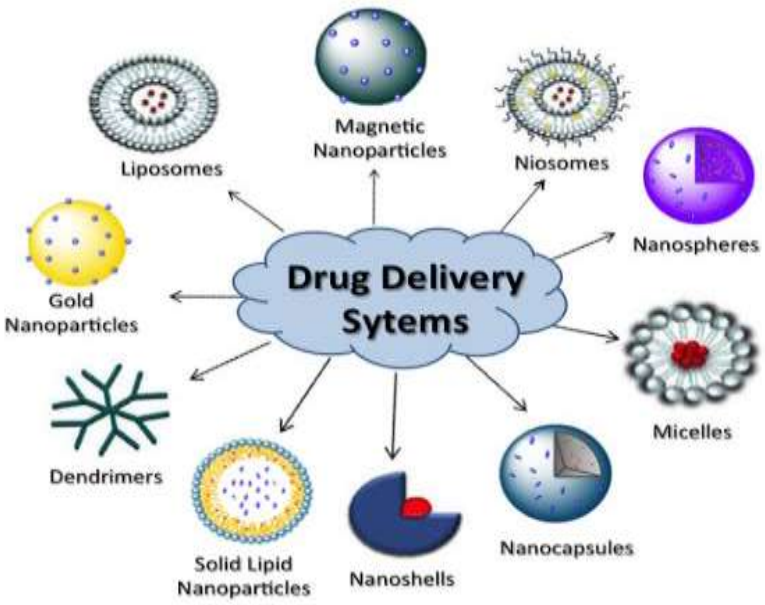

Figure: 01.

These nanotechnologies offer various advantages, including improved drug solubility, controlled release, targeted delivery, and reduced side effects. The choice of nanotechnology depends on the specific characteristics of the drug, the desired therapeutic effect, and the intended route of administration.[58]

Nanoparticle-Based Drug Delivery: Nanoparticles continue to be a focus in drug delivery due to their unique properties, such as small size, large surface area, and the ability to encapsulate various drugs. Liposomes, polymeric nanoparticles, and lipid-based nanoparticles are commonly studied for drug delivery applications.[26]

Targeted Drug Delivery: Researchers are increasingly focusing on developing targeted drug delivery systems to enhance the therapeutic efficacy of drugs while minimizing side effects. Ligand-conjugated nanoparticles are designed to target specific cells or tissues, improving drug delivery precision.[27]

Controlled Release Systems: Advancements in controlled release systems aim to provide sustained drug release over extended periods, improving patient compliance and reducing the frequency of administration. Responsive or stimuli-sensitive nanoparticles release drugs in response to specific environmental triggers, such as pH, temperature, or enzymatic activity.

Nanotechnology in Cancer Treatment: Nanoparticles are extensively investigated for cancer drug delivery to enhance drug accumulation at tumor sites, reducing systemic toxicity. Personalized medicine approaches involve tailoring drug delivery systems based on individual patient characteristics.[34]

Gene Delivery Systems: Nanoparticles are explored for delivering genetic material, such as DNA or RNA, for gene therapy applications. CRISPR/Cas9 technology is being integrated into some nanoparticle delivery systems for targeted gene editing.

Biodegradable Nanoparticles: Development of biodegradable nanoparticles is a key area of interest to improve the safety profile of drug delivery systems. Materials such as poly (lactic-co-glycolic acid) (PLGA) are commonly used due to their biocompatibility and biodegradability.

Innovations in Administration Routes: Advancements in non-traditional administration routes, such as transdermal, nasal, or ocular delivery, are being explored for specific drug classes.

Combination Therapies: Nanoparticles are employed for combination therapies, where multiple drugs or therapeutic agents are delivered simultaneously to enhance treatment outcomes.

Improving drug bioavailability and patient compliance is crucial for enhancing the effectiveness of pharmaceutical treatments. Here are some applications and strategies for achieving these goals:

Nanotechnology in Drug Delivery

Nanoformulations: Utilize nanotechnology to create drug formulations with improved bioavailability. Nano-sized drug carriers can enhance solubility, stability, and absorption, leading to increased bioavailability.

Targeted Delivery Systems: Design nanoparticles or liposomes to target specific tissues or cells, ensuring the drug reaches its intended site of action. This reduces side effects and enhances therapeutic outcomes.[30]

Prodrug Design: Modify the chemical structure of drugs to create prodrugs, which are inactive or less active precursors that undergo conversion in the body to the active form. This can improve drug absorption, distribution, and bioavailability.

Formulation Enhancements

Solid Dispersions: Use techniques such as spray drying or hot-melt extrusion to create solid dispersions, improving the solubility and dissolution rate of poorly water-soluble drugs.(29)

Micronization: Reduce drug particle size to enhance dissolution rates and increase surface area for absorption.

Modified Release Formulations

Controlled Release: Develop extended-release formulations to maintain therapeutic drug levels over a more extended period, reducing the frequency of dosing and improving patient compliance.

Gastric Retentive Systems: Design formulations that prolong gastric residence time, optimizing drug absorption and bioavailability.

Combination Therapies

Fixed-Dose Combinations: Combine multiple drugs with complementary mechanisms of action into a single dosage form, improving patient compliance by simplifying the treatment regimen.

Synergistic Drug Combinations: Explore synergistic drug combinations that enhance therapeutic efficacy, allowing for lower individual doses and potentially reducing side effects.

Patient-Friendly Dosage Forms

Orally Disintegrating Tablets (ODTs): Create fast-dissolving tablets that dissolve quickly in the mouth without the need for water, improving ease of administration and patient compliance.

Liquid Formulations: Develop liquid formulations for patients who have difficulty swallowing solid dosage forms, such as pediatric or geriatric populations.

Digital Health Solutions

Smart Pill Technologies: Integrate digital sensors into drug formulations to monitor adherence and provide real-time feedback to healthcare providers.

Mobile Health Apps: Develop mobile applications that provide medication reminders, educational resources, and tracking features to enhance patient engagement and compliance.

Patient Education and Counseling

Health Literacy Programs: Implement educational initiatives to improve patients' understanding of their medications, dosing regimens, and the importance of adherence.

Communication Tools: Use various communication channels, including telehealth, to facilitate ongoing dialogue between healthcare providers and patients, addressing concerns and promoting adherence.

By employing these strategies, pharmaceutical companies and healthcare professionals can contribute to better drug bioavailability, increased patient compliance, and ultimately improved therapeutic outcomes.[29]

NANOEMULSIONS

Inayat Pathan et al developed a nanoemulsion for the transdermal drug delivery of meloxicam. The area of nanoemulsion was identified by constructing a pseudo ternary phase diagram. Nanoemulsions evaluated by Transmission electron microscopy, In-vitro Permeation study, Droplet size distribution, Stability studies, and Refractive index results concluded, that prepared nanoemulsions Are promising vehicles for transdermal delivery of meloxicam to treat pain or inflammation in the treatment of rheumatoid arthritis. Nanoemulsions droplet size was found to be in the range from 60.6 nm to -195.5 nm.[28]

FUNDAMENTALS OF NANOTECHNOLOGY-BASED TECHNIQUES IN DRUG DESIGNING

Nanodrug is the branch of drug that utilizes the wisdom of nanotechnology in the preclusion and cure of colorful conditions using nanoscale accouterments, similar to biocompatible liposomes, micelles[17], and nanorobots[18], medicine designed on the base of nanoparticles for medicine delivery similar as size and face parcels. Nanoparticles, generally in the range of 1-100 nanometers, offer a high face area-to-volume rate and unique physicochemical parcels. Face revision can be acclimatized for specific commerce with natural realities. Medicine encapsulation nanoparticles can reprise medicines, guarding them against declination and easing controlled release. This helps in perfecting medicine bioavailability and reducing side goods. Targeted delivery functionalization of nanoparticles allows for targeted medicine delivery to specific cells or napkins, adding remedial efficacity while minimizing systemic toxin. Medicine designed on the base of nanostructure–grounded medicine expression similar to liposomes lipid grounded nanocarriers, liposomes enhance the solubility of inadequately water-answerable medicine. Liposomes can also be designed for targeted medicine release. Biocompatible polymers like PLGA (poly lacticco-glycolic acid) are used to produce nanoparticles. They offer sustained medicine release and are customizable of colorful medicine types. Micelles amphiphilic motes tone- assemble into micelles, which can synopsize hydrophobic medicines in their core. This structure enhances medicine solubility and stability. Medicine designing on the base of individual nanotechnology similar as amount blotches these semiconductor nanocrystals have unique optic parcels and are used in imaging and diagnostics. They can be finagled to emit specific wavelengths, abetting in targeted imaging and early complaint discovery. For colorful operations including, opinion[19], delivery[20], sensitive actuation purposes in a living organism.[21] still, the efficacity of these nanostructures as medicine delivery vehicles vary depending on the size, shape, and other

essential biophysical/ chemical characteristics. For case, polymeric nanomaterial's with compasses ranging from 10 to 1000 nm, parade characteristics ideal for an effective delivery vehicle.[22]

NANOMATERIALS IN MEDICINE NEEDS

Nanomaterials play a crucial role in medicine and have shown great promise in various applications. Here are some of the significant needs and potential uses of nanomaterials in medicine:

Targeted Drug Delivery: Nanomaterials can be engineered to deliver drugs specifically to targeted cells or tissues, minimizing side effects and increasing therapeutic efficiency.

Controlled Release: Nanoparticles can release drugs in a controlled and sustained manner, improving the drug's efficacy and reducing the frequency of administration.

Diagnostic Imaging: Nanomaterials can enhance imaging techniques such as MRI, CT scans, and ultrasound, providing higher resolution and improved contrast for better diagnostics.

Theranostics: Nanomaterials can be designed to simultaneously diagnose and treat diseases, offering a personalized approach to medicine.

Gene Therapy: Nanoparticles can deliver therapeutic genes to target cells, offering potential treatments for genetic disorders.

Photothermal Therapy: Nanomaterials, such as gold nanoparticles, can absorb light and convert it into heat, allowing for targeted destruction of cancer cells.

Hyperthermia Treatment: Magnetic nanoparticles can generate heat when exposed to a magnetic field, which can be used for localized hyperthermia treatment of tumors.

Biosensors: Nanomaterial-based biosensors enable early detection of diseases by detecting specific biomarkers, paving the way for timely intervention and treatment.

Point-of-Care Testing: Portable nanosensors can be employed for rapid and on-site diagnostics, particularly in resource-limited settings.[32]

Regenerative Medicine

Tissue Engineering: Nanomaterials can be used to create scaffolds that mimic the extracellular matrix, promoting cell adhesion and tissue regeneration.

Stem Cell Therapy: Nanomaterials can enhance the delivery and viability of stem cells, improving their therapeutic potential in regenerative medicine.

Improved Vaccine Delivery: Nanoparticles can be used to deliver vaccines, enhancing their stability, efficacy, and immune response.

Adjuvants: Nanomaterials can act as adjuvants, boosting the immune response to vaccines.
Drug-Resistant Infections: Nanomaterials can be used to develop novel antimicrobial agents for combating drug-resistant bacteria and viruses.

Diagnostic Tools

Biosensing Platforms: Nanomaterial-based biosensors can be used for the rapid and sensitive detection of various biomolecules, aiding in disease diagnosis.

Despite these promising applications, it's important to consider the potential toxicity and long-term effects of nanomaterials in the human body. Research and development in this field are ongoing to ensure the safe and effective use of nanomaterials in medical applications.[33]

DESIGNING OF DRUG

Drug designing of nanoparticles involves the intentional design and optimization of nanoscale drug delivery systems to enhance the therapeutic efficacy of drugs. Here is a step-by-step overview of the drug designing process for nanoparticles.[59]

1. Identification of Target and Disease (Identify the specific molecular targets associated with the disease. Understand the physiological and pathological characteristics of the target site.)
2. Selection of Nanoparticle Materials (Choose appropriate materials for nanoparticle construction. Common materials include lipids, polymers, and inorganic materials. Consider factors such as biocompatibility, biodegradability, and stability.)
3. Nanoparticle Formulation (Determine the type of nanoparticles (liposomes, polymeric nanoparticles, micelles, etc. suitable for the specific drug and target. Optimize the size, shape, and surface properties of nanoparticles for effective drug delivery)
4. Drug Loading (Encapsulate the drug within the nanoparticles or attach it to the nanoparticle surface. Optimize drug loading to achieve a balance between therapeutic efficacy and potential toxicity.[60]
5. Controlled Drug Release (Design nanoparticles with controlled release mechanisms. Consider factors like sustained release, triggered release (pH, temperature, enzymatic triggers), or pulsatile release.)
6. Targeting Strategies (Passive Targeting: Leverage the enhanced permeability and retention (EPR) effect for preferential accumulation in target tissues. Active Targeting: Attach ligands (antibodies, peptides) to nanoparticles for specific recognition of target cells, enhancing uptake.)

7. Biocompatibility and Toxicity Assessment (Conduct thorough studies to ensure the biocompatibility of the nanoparticle formulation. Evaluate potential toxicity through in vitro and in vivo studies.)
8. Stability and Storage Considerations (Optimize the stability of nanoparticle formulations to prevent aggregation or degradation. Develop appropriate storage conditions to maintain the integrity of the nanoparticles.[61]
9. Scale-Up and Manufacturing (Develop scalable processes for the large-scale production of nanoparticles. Implement quality control measures to ensure consistency in nanoparticle characteristics.)
10. In vitro Studies (Evaluate the performance of nanoparticle-drug formulations in cell culture studies. Assess cellular uptake, cytotoxicity, and intracellular drug release.)
11. In vivo Studies (Assess the pharmacokinetics and biodistribution of nanoparticles in animal models. Evaluate the therapeutic efficacy and safety of the nanoparticle-drug system.
12. Clinical Trials (Conduct clinical trials to evaluate the safety, efficacy, and pharmacokinetics of the nanoparticle-based drug delivery system. Optimize the formulation based on feedback from clinical trials.)
13. Regulatory Approval (Compile data on the safety and efficacy of the nanoparticle-based drug delivery system for regulatory submission
14. Post-Marketing Surveillance (Continuously monitor the performance of the nanoparticle-based drug in real-world settings. Address any emerging safety or efficacy concerns.[62]

Throughout this process, interdisciplinary collaboration among scientists, engineers, pharmacologists, and clinicians is essential to ensure the success of nanoparticle-based drug delivery systems. The field of nanomedicine continues to evolve, with ongoing research aiming to improve the design, targeting, and therapeutic outcomes of nanoparticle formulations.[63]

DRUG DELIVERY PROCESS

The drug delivery process involves the administration of therapeutic substances to achieve a desired pharmacological effect in the body. It encompasses various methods and technologies to deliver drugs in a controlled and targeted manner. Here's an overview of the drug delivery process.[64]

1. Drug Formulation (Develop a pharmaceutical formulation of the drug that is suitable for administration. Consider the physical and chemical properties of the drug, such as solubility, stability, and bioavailability.)
2. Dosage Form Design (Determine the appropriate dosage form, such as tablets, capsules, injections, patches, or inhalers. Consider patient factors, convenience, and the desired rate of drug release.)
3. Drug Administration Routes (Oral administration common and convenient. Affords absorption through the gastrointestinal tract. Parenteral administration injecting the drug directly into the body, including intravenous, intramuscular, and subcutaneous routes. Topical administration application on the skin for local effects. Pulmonary Administration: Inhalation for rapid absorption through the lungs. Transdermal administration absorption through the skin for systemic effects.[65]
4. Drug Absorption (Understand the absorption characteristics of the drug based on its physicochemical properties. Consider factors such as permeability, solubility, and stability.)
5. Distribution (Assess how the drug is distributed within the body after absorption. Consider factors like blood circulation, tissue perfusion, and drug binding to plasma proteins.)
6. Metabolism (Understand how the drug is metabolized by the body, usually in the liver. Evaluate the formation of active or inactive metabolites.)
7. Excretion (Consider the elimination of the drug and its metabolites from the body, often through the kidneys (urine) or liver (bile).
8. Controlled Release Systems (Design formulations that control the rate and timing of drug release. Types include sustained release, extended release, and pulsatile release systems.[66]
9. Targeted Drug Delivery (Passive targeting exploit physiological properties, such as the enhanced permeability and retention (EPR) effect, for selective drug accumulation. Active targeting utilize ligands or antibodies to target specific cells or tissues, improving drug delivery precision.)
10. Drug Carrier Systems (Use carrier systems like liposomes, nanoparticles, or micelles to enhance drug solubility, stability, and targeting.[67]
11. Monitoring and Optimization (Employ imaging techniques and biomarkers to monitor drug distribution and therapeutic effects. Continuously optimize formulations for better efficacy and reduced side effects.)

12. Patient Adherence (Consider factors that may affect patient adherence, such as the dosing schedule and ease of administration.)
13. Safety and Efficacy Evaluation (Conduct preclinical and clinical studies to assess the safety and efficacy of the drug delivery system. Collect data for regulatory approval.)
14. Regulatory Approval (Submit data to regulatory authorities for approval.)
15. Post-Marketing Surveillance (Monitor the drug's performance in real-world settings. Address any emerging safety or efficacy concerns.[68]

The drug delivery process is an interdisciplinary field that involves collaboration between pharmacologists, chemists, engineers, and clinicians. Continuous advancements in technology and research contribute to the development of innovative drug delivery systems with improved therapeutic outcomes and patient compliance.[70]

MECHANISM OF NANOPARTICLES

The mechanism of nanoparticles in drug delivery involves several key aspects, including their unique physical and chemical properties that enable targeted and controlled drug release. Here's an overview of the mechanisms underlying nanoparticle-based drug delivery.[69]

1. Enhanced Permeability and Retention (EPR) Effect(Nanoparticles can exploit the EPR effect, which is characterized by the leaky vasculature and impaired lymphatic drainage in certain tissues, especially tumor tissues. The EPR effect allows nanoparticles to passively accumulate in target tissues, enhancing drug delivery to specific sites.)
2. Size-Dependent Drug Delivery (Nanoparticles typically have sizes in the nanometer range, allowing them to interact with biological structures at the cellular and subcellular levels. The small size facilitates improved tissue penetration and cellular uptake.
3. Surface Modification and Functionalization (Nanoparticles can be functionalized with specific ligands, antibodies, or peptides on their surfaces. Surface modification enables active targeting by recognizing and binding to specific receptors on target cells, enhancing drug delivery precision.)
4. Cellular Uptake (Nanoparticles can enter cells through various mechanisms, such as endocytosis or direct penetration through the cell membrane. Internalization allows nanoparticles to release the encapsulated drug inside the target cells.)
5. Intracellular Drug Release (Once inside the target cells, nanoparticles can release the drug payload through processes like endosomal escape or controlled release mechanisms. The release kinetics can be designed to match the therapeutic requirements.)

6. Biodegradation and Metabolism (Biodegradable nanoparticles are designed to undergo degradation over time, releasing the drug payload gradually. Metabolism may involve enzymatic processes that break down the nanoparticle structure).
7. Avoiding Immune System Recognition (Surface modifications can be employed to reduce recognition by the immune system, minimizing clearance and extending circulation time in the bloodstream).
8. Biodistribution and Pharmacokinetics (Nanoparticles can alter the biodistribution and pharmacokinetics of drugs by modifying their release profiles and systemic circulation. The size, shape, and surface charge of nanoparticles influence their interaction with biological barriers and clearance by the reticuloendothelial system).[31]
9. Responsive Drug Release (Nanoparticles can be designed to respond to specific environmental stimuli, such as changes in pH, temperature, or enzymatic activity. Responsive release mechanisms enable controlled drug release at the target site.
10. Theranostic Applications (Nanoparticles can be used for both therapeutic and diagnostic purposes (theranostics).

Incorporating imaging agents allows monitoring of nanoparticle biodistribution and therapeutic response.

11. Carrier Systems

Nanoparticles serve as carrier systems for poorly soluble drugs, improving drug solubility and bioavailability.

Understanding these mechanisms allows researchers to design and optimize nanoparticle-based drug delivery systems for specific therapeutic applications, enhancing the efficacy and reducing side effects of various drugs. Ongoing research in nanomedicine continues to explore innovative approaches for improving the performance of nanoparticle drug delivery systems.[31]

Continuous Delivery System Based Upon The Osmotic Property

Thin flat layer, contoured three-dimensional unit. Conform to the space of the upper conjunctival Fornix. Delivery of diethyl carbamazepine in ocular onchocerciasis.

Lipid Nanoparticles

Compactly, solid lipids and hydrophobic medicines are dissolved in a water- immiscible organic detergent(e.g., cyclohexane, toluene, and chloroform), which is also dispersed in an waterless result to form oil painting- in- water mixes. Also LNPs are generated as a result of the evaporation of organic detergent. Common synthetic polymeric nanoparticles include polyacrylamide, polyacrylate, and chitosan. Medicine motes can be incorporated either during or after polymerization. Depending on the polymerization chemistry, the medicine can be covalently clicked, reprised in a hydrophobic core, or conjugated electrostatically Study using nanosphere done on a system Constituted of pilocarpine- loaded nanosphere of Polymethylmethacrylate acrylic acid copolymer By Gurney et another study list of Pilocarpine to poly butyl cyanoacrylate Nanoparticles enhanced the miotic. Developed pH sensitive Nanoparticles for pilocarpine and the result was set up to be promising. In response by about 22 to 33.[23]

Nanoparticles and drug delivery

Drug delivery and related pharmaceutical development In the context of Nanomedicine should be viewed as the science and technology of nanometer-scale complex systems (10–1000 nm), consisting of at least two components, one Of which is a pharmaceutically active ingredient (Duncan 2003; Ferrari 2005), although nanoparticle formulations of The drug itself are also possible (Baran et al 2002; Cascone Et al 2002; Duncan 2003; Kipp 2004). The whole system Leads to a special function related to treating, preventing, or diagnosing diseases sometimes called smart drugs or the agnostic (LaVan et al 2003). The primary goals for research of Nano-bio-technologies in drug delivery Include:

- More specific drug targeting and delivery,
- Reduction in toxicity while maintaining therapeutic Effects,
- Greater safety and biocompatibility, and
- Faster development of new safe medicines

Use of NP formulations in drug delivery

One of the major challenges in drug delivery is to get the drug at the place it is needed in the body thereby avoiding potential Side effects to non-diseased organs. This is especially challenging in cancer treatment where the tumor may be localized as distinct metastases in various organs. The non-restricted (cyto) toxicity of chemotherapeutics thus limits the full use of their therapeutic potential.

Need for a Dosage Form

Generally, drug delivery systems (DDS) are preferred because direct clinical use of the active drug substances (APIs) "as they are" is very rare due to several reasons: API handling and accurate dosing can be difficult or impossible for very potent drugs (e.g., low mg and µg doses).[35]

Biopharmaceutics System (BCS) Classification of Drugs: Biopharmaceutical classification system (BCS) is an advanced tool used for classifying drug substances on dissolution, intestinal permeability and water solubility.[36]

Drug Disposition

The significant route of elimination of drugs showing high intestinal permeability in humans is mainly by metabolism and the drugs having weak intestinal permeability rates are mainly excreted as unchanged drugs in the urine and bile in humans. In 2005 drug disposition was first observed by Wu and Benet 43.[71]

ALTERNATE ROUTE OF DRUG

Delivery Intranasal drug delivery

In addition to being convenient and painless, there is no reduction in the bioavailability of drugs administered nasally.[37]Direct deliveries to the cerebrospinal fluid due to the nose-brain Pathway reduce the onset time. Highly lipophilic drugs of low Molecular weight easily cross the nasal mucosa.[38-39]

Pulmonary drug delivery system

Pulmonary drug delivery system: Metered dose inhalers, nebulizers, and dry powder inhalers Are used for pulmonary drug delivery.[40] They offer several Advantages including a larger surface area and closer proximity To blood flow.[40-41]

Transdermal drug delivery system

Transdermal drug delivery system: Reservoir patches and matrix patches are the two types of patches.[42] There is no background infusion and passive absorption of the drug is negligible. Ahmad et al. compared intravenous patient-controlled analgesia morphine with fentanyl iontophoretic transdermal system and found the latter to be associated with lesser analgesic gaps.[43-44]

Strategies for drug delivery to the brain : Several drugs do not have adequate physiochemical characteristics Such as high lipid solubility, low molecular size and positive Charge which are essential to succeed in traversing BBB.[21]

Disruption of the BBB

The allowed behind this approach was to break down the hedge shortly by edging in mannitol result into highways in the Neck. The performing high sugar attention in brain capillaries takes up water out of the endothelial cells, shrinking them, therefore Opening tight junctions. The effect lasts for 20- 30 twinkles, during which time medicines verbose freely, which would not typically cross the BBB. This system permitted the delivery of chemotherapeutic agents in cases with cerebral carcinoma, nasty glaucoma, and circulated CNS origin cell excrescences. Physiological stress, flash increase in intracranial pressure, and unwanted delivery Of anticancer agents to normal brain apkins are the uninvited side goods of this approach in humans.[45]

Natural product - grounded nanotechnology and medicine Delivery

As per the World Health Organization(WHO) report, in developing countries, the introductory health requirements of roughly 80 of the population are met and/ or rounded by traditional drug.(46)Presently, these natural product- grounded accoutrements are considered the crucial constituents in the medication and Processing of new Nano- phrasings because they've intriguing characteristics, similar as being biodegradable, biocompatible, available, renewable, and Presenting low toxin(47-48). In addition to The afro variations mentioned parcels, biomaterials are, for the utmost part, able of witnessing chemical, Guaranteeing them unique and desirable parcels for Is implicit uses in the field of Nanomedicine. Gold, tableware, cadmium sulfide, and titanium dioxide of Different morphological characteristics have been synthesized using a number of bacteria videlicet Escherichia Coli, Pseudomonas aeruginosa, Bacillus subtilis and Klebsiellosis pneumoniae. These nanoparticles, especially gray nanoparticles have been abundantly studied In vitro for their antibacterial, antifungal, and cytotoxicity eventuality due to their advanced implicit among all essence Nanoparticles.[49-50] In the event of microorganism- intermediated nanoparticle conflation, maximum exploration is concentrated on the way that microorganisms reduce essence Precursors and induce the nanoparticles. For case, Rahimi etal.[51]

Microemulsions

Microemulsions are novel ocular delivery systems that are mainly dispersions of water and oil along with a surfactant. Microemulsions confer advantages such as higher thermodynamic stability, improved solubility, and improved corneal Permeation. The critical parameters that affect the stability of the microemulsion system are the selection of aqueous phase, Organic phase, and surfactant/cosurfactant systems. Cyclosporine A was formulated with microemulsions made of Brij 97 and loaded into 2-hydroxyethyl methacrylate (p-HEMA) hydrogels. Release of cyclosporine from these formulations was observed for a period of 20 days in an in-vitro release study. A microemulsion-based phase transition system was Developed and evaluated for the ocular delivery of pilocarpine hydrochloride. This system used sorbitan monolaurate and Polyoxyethylenesorbitan mono-oleate, which are nonionic surfactants with ethyl oleate, the oil component, and water. The system undergoes various phase transitions with changes in viscosity depending on water content.[52-54]

NANOPARTICLES INVOLVED IN DRUG DELIVERY SYSTEMS

Common synthetic polymeric nanoparticles include polyacrylamide, polyacrylate, and chitosan. Drug molecules can be incorporated either during or after polymerization. Depending on the polymerization chemistry, the drug can be covalently bonded, encapsulated in a hydrophobic core, or conjugated electrostatically.[53]

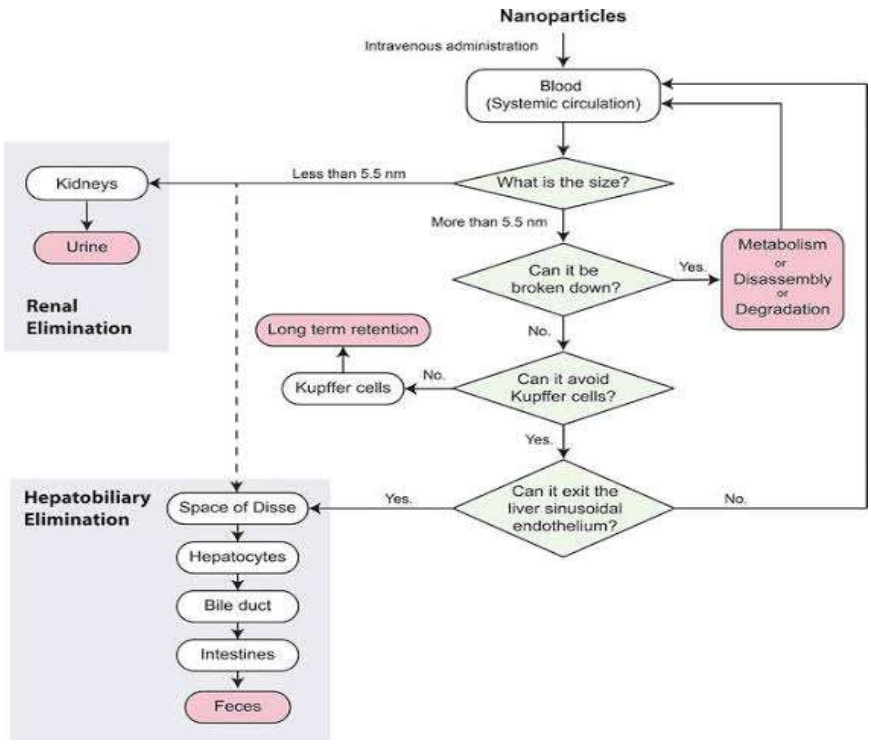

Figure 02.

CONCLUSION

The recent developments in medicine delivery systems, especially those involving nanoparticles, showcase a growing emphasis on perfection, targeted remedies, and bettered patient compliance. As the field advances, it holds a great pledge to revolutionize the way medicines are administered and optimize remedial issues. Experimenters are decreasingly concentrated on addressing challenges and refining these technologies for broader clinical operations. For the most recent developments, it's essential to consult the rearmost scientific literature and exploration publications. A new medicine delivery system is a volition to the conventional styles of administering medicines. To treat a case, an ultramodern drug first determines where in the body the complaint is manifesting and also delivers the drug directly to the area of the body where it'll have the most effect. The nonstop development and refinement of medicine delivery systems, especially those involving nanoparticles, hold great eventuality for revolutionizing medical treatments. Advanced bioavailability, targeted delivery, and enhanced patient compliance contribute to the overall efficacity and safety of remedial interventions. As exploration progresses, we will likely see indeed more sophisticated and acclimatized medicine delivery approaches, addressing specific challenges associated with different conditions and patient populations. The nonstop elaboration of medicine delivery systems, particularly with the integration of nanoparticles, has significantly enhanced medicine bioavailability and case compliance. These advancements offer targeted and sustained medicine release, bettered stability, and substantiated treatment options. As exploration and development in this field progress, it's likely that we will see indeed more sophisticated and patient-centric medicine delivery results in the future. It's important to consult the rearmost scientific literature for the most recent developments in this fleetly advancing field.

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