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Nano-Drug Delivery Systems Of Bioavailability And Bioactivity

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Abstract

Bioavailability refers to the fraction of administered drug that reaches the systemic circulation in an unchanged form and is available to exert its therapeutic effects. It is the rate and extent to which a drug is absorbed from its dosage form and becomes available at the site of action. Bioavailability and bioactivity both the concepts are related to the effectiveness of drugs. The term pharmacological response is directly related to our body's blood plasma levels.

Thus, bioavailability is defined as the rate and extent (amount) of absorption of an unchanged drug from its dosage form. An ideal drug must have to live within the body and must not reform the properties of biomolecules apart from target molecules. Nano drug delivery systems, also known as nanocarriers or nanomedicines, refer to a class of pharmaceutical formulations that utilize nanotechnology to deliver drugs or therapeutic agents to specific target sites within the body. Nanotechnology offers precise control over the design and fabrication of drug delivery systems. By encapsulating drugs within nanoparticles or nanocarriers, their stability, solubility, and targeted delivery can be improved. Nanoparticles can protect drugs from degradation, enhance their absorption, and enable controlled release, thus improving bioavailability.

Nanoparticles can be engineered to specifically target diseased cells or tissues while sparing healthy ones. Functionalized nanoparticles can be designed to attach to specific molecules or receptors found on cancer cells, for instance. This targeted approach reduces systemic side effects and enhances the bioactivity of therapeutic agents.

Keywords: Nano Drug delivery system, Bioavailability, Nanocarriers, Bioactivity, Nanotechnology.

I. INTRODUCTION

A drug which is obtained from plant, animal or any other synthetic sources exerts its therapeutic efficacy by delivering its active medicaments to specific site of action to obtain required pharmacological response.

Mostly, drugs acts by binding with targeted receptors or enzymes and inhibiting or otherwise transforming their pharmacological activities. The therapeutic result of any constituents may be obtained from numerous sources which depend upon the criteria to deliver the medicament to its site of action at a specific rate to exert the desired pharmacological response.

The ability of the dosage form to elicit its therapeutic response is termed as physiologic availability, biological availability, or sometimes simply as bioavailability [1]. Bioavailability refers to the extent and rate at which a drug or a substance is absorbed into the bloodstream and becomes available at the site of action or metabolism. In other words, it is a critical concept of pharmacology, as it directly influences the pharmacological effectiveness of a drug. Bioavailability and bioactivity both the concepts are both related to the effectiveness of drugs.

The term pharmacological response is directly related to our body's blood plasma levels. Thus, bioavailability is defined as the rate and extent (amount) of absorption of an unchanged drug from its dosage form.

An ideal drug must have to live within the body and must not reform the properties of biomolecules apart from target molecules [2]. They are wielded to treat almost all diseases and save human beings in fight against numerous infectious diseases and widespread [3].

Modern drug dosage forms have evolved significantly to provide more effective and convenient ways of treating diseases. In spite of all these, some more common problems associated with these dosage forms like their efficacy, bioavailability, bioactivity, toxicity, biocompatibility, side-effects, and inactivity problems are the drug development process [4]. It's essential to consider these limitations and tailor the choice of dosage form to the specific needs and characteristics of each patient and medication. In recent days, advancement in drug delivery technologies continues to address various highly sophisticated engineered nanoparticles that have been exploited to overcome these problems and enhance overall treatment.

A drug-delivery system (DDS) is a formulation or device that allows the introduction of active ingredients into the body in order to improve not only their efficacy but also their safety, by controlling the drug amount, time, and release in the site of action, crossing the biologic membranes to get to the therapeutic target [5]. Different factors influence bioavailability such as route of administration, drug formulation, metabolism, and excretion. Different routes of administration have different bioavailability characteristics.

The most common routes of drug administration are oral (swallowing a tablet or capsule) and intravenous administration into the bloodstream which produces 100% bioavailability since the drug is directly administered into the systemic circulation. Oral administration has lower bioavailability due to factors such as incomplete absorption in the gastrointestinal tract and first-pass metabolism in the liver [6].

Bioactivity is concerned with the drug's ability to produce the intended biological response. There are some common attributes that create challenges for DDS related to bioavailability.

- **Poorly Soluble Drugs:** Drugs with low water solubility may have limited dissolution in the gastrointestinal tract, leading to poor absorption and reduced

bioavailability. DDS must address strategies to enhance drug solubility or employ alternative routes of administration.

- **First-Pass Metabolism:** Drugs administered orally are subject to first-pass metabolism in the liver before reaching the systemic circulation. This can significantly reduce bioavailability. DDS can aim to bypass first–pass metabolism through alternative routes or develop prodrugs that undergo less metabolism.

- **Gastric Degradation:** Some drugs are susceptible to degradation in the acidic environment of the stomach, reducing their bioavailability. DDS must protect drugs from gastric degradation or use alternative routes of administration.

- **Fast Excretion:** The fast excretion process refers to the rapid removal of waste products and toxins from the body. This is facilitated by organs like the kidneys, which filter blood to remove waste and excess substances, producing urine that is then excreted from the body. The body's efficiency in eliminating waste

is crucial for maintaining overall health and preventing the buildup of harmful substances [7].

- **Fraction of Drug Required Zone:** Some specific tumor cells require more amount of drug accumulation in our body, which is high as compared to normal cells for effective cancer treatment [8].

Bioactivity is an approach that refers to the ability of a drug to exert its intended pharmacological or therapeutic effect on the target site of action. In other words, it is the drug's ability to bind to its receptor or target and initiate the desired physiological response. The bioactivity associated with drug delivery symptoms refers to the issue of maintaining the therapeutic efficacy of the drug throughout the delivery process [9].

The current challenges associated with drug development and delivery which pharmaceutical companies are facing related to bioactivity is

- **Targeting Specificity:** The drug should be delivered specifically to the target site to maximize bioactivity and minimize off target effects. Achieving precise targeting is challenging especially when dealing with complex biological barriers and heterogeneous diseases.

- **Drug Stability:** Many drugs are sensitive to environmental conditions, such as temperature, light, and humidity, which can cause degradation and loss of bioactivity. Ensuring the stability of the drug within the DDS during storage and transportation is crucial.

- **Drug Release Kinetics:** Controlling the rate and duration of drug release from the DDS is essential to achieve the desired therapeutic effect. If the drug is released too quickly, it may lead to adverse effects or inadequate treatment, whereas slow release may result in suboptimal bioactivity.

- **Drug Interactions:** The presence of other components within the DDS or the body, such as enzymes or other drugs, may interact with the drug and alter its bioactivity. Drug interactions can lead to reduced effectiveness or unexpected side effects.

- **Biocompatibility and Toxicity:** Some DDS materials or drug formulations may trigger immune responses or exhibit toxicity, compromising the bioactivity of the drug and potentially causing harm to the patient.

- **Patient Variability:** Differences in patient's physiology, metabolism and health conditions can influence the bioactivity of the drug delivered by the DDS. Personalized medicine approaches may be required to account for these variations.

1. Nanotechnology: Nanotechnology is a branch of advanced technology that deals with the manipulation and control of matter on an atomic and molecular scale, typically at dimensions between 1 and 100 nanometers. Nanotechnology is the science of the small. Nanotechnology has the ability to observe measure, manipulate, assemble, control, and manufacture particulate at the nanometer scale [10]. Researchers are interested in the nanoscale level due to the numerous advantages of this scale that the properties of materials can be very significantly from those at a larger scale. In the nanoscale, materials, and devices exhibit some unique properties and symptoms. Since the last decade, nanoparticles have gained popularity for applications in biology and medicine. Nanotechnology has the technical ability to retransform the various pharmacokinetic properties, biopharmaceutical properties. Depending upon the morphology, size, composition, and physical-chemical and biological properties of nanoparticles, they played a significant role in the field of drug delivery systems. Nanotechnology offers different manipulations over the drug design, drug synthesis, and fabrication of drug delivery systems. Drug stability, solubility, and targeted delivery can be improved by encapsulating that drug within nanocarriers or nano-matrix [11]. The diverse technological benefits of nanoparticles used as drug carriers are high stability, high carrier capacity, feasibility of incorporation of both hydrophilic and hydrophobic substances, etc. In the context of medicine, nanotechnology has given rise to treatment with increased bioavailability, reduces the frequency of administration, and promotes the targeting of drugs to specific sites. Nanomaterials have wider applications as a revolutionary technology across various industries for genetic tissue engineering, electronics, medical device designing, and the encapsulation and delivery of drugs, energy, and materials

science. In the recent context of the drug delivery system, the development of control release targeted drug delivery includes the presence of active drug in the target area of the body such as cancerous cells, and sustained release of the dosage form in which the drug is released over an extended period of time in a controlled manner from the dosage form [12].

2. Nanodrug Delivery System: Nano drug delivery systems, also known as nanocarriers or nanomedicines, refer to a class of pharmaceutical formulations that utilize nanotechnology to deliver drugs or therapeutic agents to specific target sites within the body. Nanotechnology in medicine concept was first evolved by Dr. Richard P. Feynman

in the year of 1950. One of the most diverse applications of nano in medicine is in drug delivery systems. It is recently hypothesized that most conventional DDS have poor bioavailability and low aqueous solubility limiting their absorption and retention within biological systems. However, these nano-drug delivery systems are designed to improve the efficacy and safety of drug delivery by enhancing the drug's pharmacokinetic properties, reducing side effects, and increasing drug bioavailability and bioactivity. Nano-drug delivery systems (NDDS) are complex and diversified systems. some common features associated with NDDS are specified below [13].

- **Particle Size:** Nanoparticles used in NDDS typically have a size range of 1 to 100 nanometers. This small size helps in vivo distribution, biological profile, toxicity studies, and targeting ability of these nano delivery systems. Moreover, Nanosize immensely promotes drug loading, drug release, and stability profile. It has been reported that nanomaterials due to their small size allows for enhanced permeability and retention effect, enabling them to accumulate in tumor tissues [14].

- **Surface Modification:** Nanoparticles surface charge is usually measured in terms of the nanomaterials zeta potential which reflects the electrical charges of particles [15]. Drug loading also depends on surface charge. Surface charges can be modified with ligands, antibodies, or other molecules to enhance targeting and interaction with specific cells or tissues. This helps improve the selectivity of drug delivery [16].

- **Drug Loading Capacity:** A highly efficient capability of nano drug delivery systems is that they have a high drug-loading capacity without aggregation. High drug loading capacity can be determined by certain factors such as the type of nanoparticle, drug, and manufacturing processes. More drug loading results in decreasing the administration of frequency of doses [17]. Efficient drug loading and high entrapment efficiency directly rely on several factors like drug solubility in the nanoparticles, dispersible medium, drug molecular weight (MW), etc. Surfaces can be modified with ligands antibodies, or other molecules to enhance targeting and interaction with specific cells or tissues. [18].

- **Targeting:** Active Targeting involves attaching ligands or antibodies to the nanoparticle surface that can recognize specific receptors on the target cells, improving chemotherapy by nanomaterials availing a highly specific cancer treatment. Active or passive targeting mechanisms can be incorporated to direct the NDDS to specific cells or tissues. Ligands or antibodies might be used for active targeting [19].

- **Stability:** NDDS should maintain their structure and drug cargo stability during storage and transportation.

- **Biodegradability:** Biodegradable NDDS can be designed in a controlled manner after releasing their payload, minimizing long-term accumulation.

- **Release Kinetics:** NDDS can be engineered to release drugs in a controlled manner, which can be tuned based on the nanoparticle material and design. This controlled release can lead to prolonged therapeutic effects and reduced side effects.

3. Different Nano Drug Delivery Systems: There are several types of nano-drug delivery systems that have been developed and studied for efficient drug delivery. Here are some commonly used nano-drug delivery systems.

- **Liposomes:** Liposomes are spherical vesicles composed of lipid bilayers. They can encapsulate both hydrophobic and hydrophilic drugs within their core or lipid layers. Liposomes offer excellent biocompatibility, controlled drug release, and the ability to target specific tissues. They have been extensively studied for drug delivery in various applications [20].

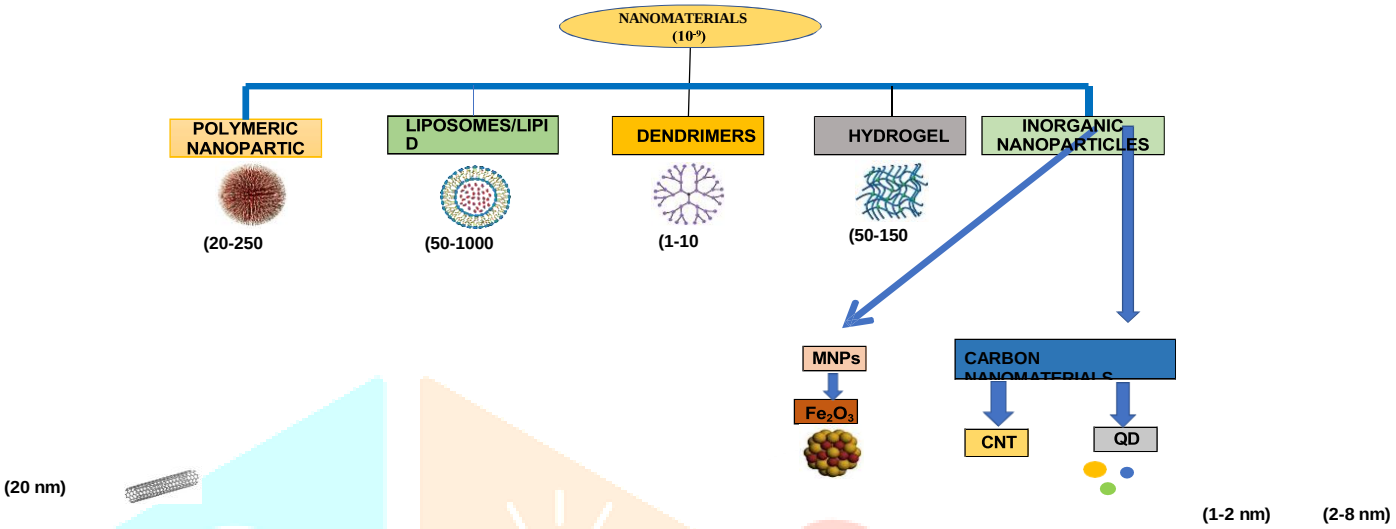

Figure 1: Classification of Different Nano Drug Delivery Formulations

- **Polymeric Nanoparticles:** These types of nanoparticles are commonly made up from biodegradable polymers. They have the ability to improve the stability and time of circulation. Synthetic polymers have diverse characteristics like high purity and reproducibility. They have the properties of high drug efficacy and good sustained release. In context of cytotoxicity studies, they are completely biocompatible and biodegradable, suitable for numerous scale-up techniques. Polymeric nanoparticles are composed of biodegradable polymers, such as poly (lactic co glycolic acid) (PLGA) and polyethylene glycol (PEG). Polymeric nanoparticles can encapsulate drugs and provide sustained release over time. They also offer flexibility in particle size, surface modification, and drug loading, making them suitable for different drug delivery applications [21].

- **Nanocrystals:** Nanocrystals are submicron sized crystalline particles composed of drug molecules. They are typically formed using techniques such as precipitations or high –pressure homogenization. Nanocrystals improve drug solubility and dissolution rate, leading to enhanced bioavailability. They are particularly useful for poorly soluble drugs.

- **Carbon Nanotubes:** Carbon nanotubes are cylindrical structures composed of carbon atoms. They have high aspect ratios and unique mechanical and electrical properties. Carbon nanotubes can be functionalized with drugs or used as carriers to deliver therapeutics. They have shown potential in targeted drug delivery and imaging applications [22].

- **Metallic Nanoparticles:** Metallic nanoparticles, such as gold nanoparticles or silver nanoparticles, have been explored for drug delivery applications. They can be functionalized with drugs, antibodies, or other targeting moieties to achieve site- specific delivery. Metallic nanoparticles also have imaging properties that can be utilized for diagnostic purposes [23].

- **Dendrimers:** Dendrimers are highly branched macromolecules with a well-defined structure. Dendrimers are generally found in three-dimensional, nanosized, radially symmetrical molecule forms which are well-defined and homogeneous structure consisting of multiple branches. They have a core-shell architecture that can encapsulate drugs within their interior or conjugate drugs on their surface. Dendrimers offer high drug-loading capacity, precise control over size and surface functionalities, and potential for targeted delivery [24-26].

- **Mesoporous Silica Nanoparticles:** Mesoporous silica nanoparticles have a porous structure with a high surface area. They can be loaded with drugs within their porous framework and release them in a controlled manner. Mesoporous silica nanoparticles offer stability, biocompatibility, and the ability to encapsulate a wide range of drugs [26].

4. Impact of Nanodrug Delivery Systems on Bioavailability And Bioactivity

- **Drug Delivery:** Nanotechnology offers precise control over the design and fabrication of drug delivery systems. By encapsulating drugs within nanoparticles or nanocarriers, their stability, solubility, and targeted delivery can be improved. Nanoparticles can protect drugs from degradation, enhance their absorption, and enable controlled release, thus improving bioavailability.

- **Increased Surface Area:** Nanostructured materials possess a high surface-to-volume ratio, which enhances their interaction with biological systems. This increased surface area facilitates better absorption of nutrients, drugs, or therapeutic agents, thereby improving bioavailability [27].

- **Targeted Therapy:** Nanoparticles can be engineered to specifically target diseased cells or tissues while sparing healthy ones. Functionalized nanoparticles can be designed to attach to specific molecules or receptors found on cancer cells, for instance. This targeted approach reduces systemic side effects and enhances the bioactivity of therapeutic agents.

- **Improved Solubility:** Many bioactive compounds have poor solubility, limiting their absorption and effectiveness. Nanotechnology can improve solubility by formulating

these compounds into nanoscale structures, such as nanoparticles or nanosuspensions, which increase their surface area and improve their dissolution properties. This, in turn, enhances bioavailability [28].

- **Enhanced Cellular Uptake:** Nanoparticles can facilitate the cellular uptake of bioactive substances by overcoming barriers such as cell membranes. Surface modifications of nanoparticles can improve their interaction with cells, promoting efficient internalization and subsequent bioactivity.

- **Diagnostic Tools:** Nanotechnology-based sensors and imaging agents allow for highly sensitive and specific detection of biological molecules or markers associated with diseases. This enables early diagnosis and monitoring of treatment response, leading to improved bioactivity and better patient outcomes.

II. PRESENTLY AVAILABLE NANO-DRUG DELIVERY SYSTEMS

Delivery of drugs Nanoparticles are often formed of a range of biodegradable materials, including natural or synthetic polymers, lipids, metals, or both, and are typically smaller than 100 nm in at least one dimension. Larger micromolecules could be used as effective delivery and transport systems because they are less successfully absorbed by cells than nanoparticles. For therapeutic purposes, drugs can either be attached to the particle surface or integrated into the particle matrix. A drug targeting system should have control over a medication's course once it enters the biological environment. Numerous investigations have been done on nano systems with different biological properties and compositions for use in gene delivery and medicine. [29].

Recently, many delivery techniques have been developed by scientists and researchers, and some of them are still being worked on today. Soluble modern drug delivery techniques include polymers, microparticles, Microcapsules, cells, cellular ghosts, lipoproteins, liposomes, micelles, dendrimers, hydrogels, and carbon nanotubes are examples of materials that are used. By conjugating these carriers with specific antibodies that target a specific location of interest, these carriers can be targeted. They are sensitive to pH and temperature changes and have a slow rate of degradation. The two categories of drug targeting are passive targeting and active targeting. Formulations based on nanoparticles have exhibited high solubility, controlled release, and superior pharmacokinetic and pharmacodynamic characteristics, surface charge and particle size, in order to create effective nanoparticle delivery systems size and shape are crucial factors [30].

1. Nano-Drug Delivery Systems

- **Hydrogel:** For the medication, therapeutic protein or vaccination antigen encapsulation and delivery, hydrogel nanoparticles based on hydrophobic polysaccharides are used. A new system that a promising compound is an extracellular polymer called cholesterol pullulan is excreted by the fungus *Aureobasidium pullulans* [31].

- **Emulsion:** Oil, water, and a surfactant are combined to form isotropic, thermodynamically stable systems known as emulsions. They include two phases

made up of a mixture of a surfactant, with or without a co-surfactant, which is used to emulsify and stabilize a mixture of two immiscible liquids. They might contain droplets with suspensions between 5 and 100 nm. It has been suggested that using microemulsions as medication delivery devices will improve drug penetration across biological membranes. Increased medication solubility and stability, as well as simplicity and affordability of scaling up, are some benefits of microemulsions [32].

- **Micelle:** To avoid quick renal clearance, polymeric micelles frequently have a restricted distribution, which allows them to build up in cancer tissues. They have a size of roughly 100 nm. The polymeric shell also limits their interactions with non- specific biological components. These nanostructures have tremendous promise for hydrophobic drug delivery because their interior core structure enables the assimilation of hydrophobic medicines, increasing their stability and bioavailability [29].

- **Liposome:** Hydrophilic and hydrophobic chemicals completely encapsulate one or more aqueous compartments in liposomes, which are small, spherical vesicles. They might be either one or several bilayers [29].

- **Dendrimer:** These a wide range of functional groups available for heavily branching macromolecules attaching drugs, imaging agents, and targeting molecules, as well as for their absorption. The ADME (absorption, distribution, metabolism, and elimination) profile depends on a number of structural characteristics. Dendrimers are three-dimensional, monodisperse, highly bifurcated structures. These structures are great candidates due of their globular shape and ease of usage as medication delivery systems with which their surface may be functionalized in a regulated manner [33].

- **Inorganic Nanoparticles:** Nanoparticles made of inorganic materials are known as inorganic nanoparticles. They are desirable for a variety of applications, including medication administration, due to distinctive features that are physical, chemical, and visual. Examples of inorganic nanoparticles include silver, gold, iron oxide, and silica particles. Surface plasmon resonance (SPR), which metal nanoparticles like silver and gold have, is one of the distinctive properties that liposomes, dendrimers, and micelles don't have. Strong biocompatibility and versatility in terms of surface functionalization were just a couple of the advantages they showed. [34].

- **Nanocrystal:** Nanocrystals are solid, pure medicine particles with a size between 1000 nm. These are only pharmaceuticals, free of any carriers, and are frequently stabilized with polymer-based stabilizers or surfactants. They can be used for biocompatibility and safety testing, combination therapies, imaging and theranostics, controlled drug release, targeted drug delivery, and drug encapsulation [31].

- **Nanoparticles Made of Carbon:** Two major types of carbon-based nanoparticles are fullerenes and carbon nanotubes (CNTs). CNTs are one kind of allotrope. Depending on the number of sheets in concentric cylinders, single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs) are two different forms of carbon with cylindrical frameworks. At least sixty carbon atoms make up the

hollow cage structure of the carbon allotrope known as a fullerene. The Buckminsterfullerene structure of C-60 has the shape of a hollow football. These carbon units are pentagonal and hexagonal in shape. They have practical applications because of their electrical conductivity, structure, high strength, and electron affinity [35].

- **Polymeric Nanoparticles:** Organic-based polymeric nanoparticles have a small size. Depending on the technique used for preparation, these are shaped like structures made of nano capsules or nanospheres [36].

- **Lipid-Based Nanoparticles:** Lipid nanoparticles are typically spherical in shape and range in diameter from 10 to 100 nm. It is made up of a matrix of soluble lipophilic compounds and lipid that surrounds a strong core. Emulsifiers and surfactants help to stabilize the outer core of these nanoparticles. These nanoparticles are utilized in the biomedical field as cancer treatment agents, drug delivery systems, and RNA release agents [36].

- **Quantum Dot:** Quantum dots (QDs), semiconductor nanocrystals, range in diameter from 2 to 10 nm. Size affects a variety of features, including absorbance and photoluminescence. The QDs have received a lot of attention in the field of nanomedicine due to their emission in the near-infrared region (less than 650 nm), which is distinct from standard organic dyes due to minimal tissue absorption and reduced light scattering. Additionally, diverse emission colors over a broad-spectrum range can be produced when QDs of various shapes and the same light source stimulate different shapes, sizes, or compositions. [37].

- **Biopolymeric Nanoparticle:** Nanosized biopolymeric nanoparticles are made of biopolymers, which are organic polymers generated from living things. These nanoparticle biocompatibility, and biodegradability and they are suited for use in a number of biologicals and medication delivery applications due to their versatility, and low toxicity. Drugs, genes and other bioactive compounds can be packaged inside biopolymeric nanoparticles to prevent them from degrading and to enhance their transport to target areas. Several typical biopolymers are employed to create biopolymeric nanoparticles such as chitosan, alginate, gelatin, albumin, starch, and hyaluronic acid [37].

- **Nano suspensions:** They are heterogeneous, surfactant-stabilized drug particle dispersions at the nanoscale. They are effective at binding to receptors. Permit excellent wide surface area which increases their bioavailability and dissolving rate, size, and little area. When medications are ineffective, they can be utilized. Having a high molecular weight, melting point, or taking the form of salt point prevents the creation of appropriate formulas [38].

2. Ongoing Research on Nano-Drug Delivery Systems: In order to increase medicine effectiveness, reduce adverse effects, and enable tailored therapeutic delivery, ongoing research on nano drug delivery devices is an important area of interest. Over the past ten years, nanotechnology has significantly impacted the medical industry through advancements in drug delivery. Drug delivery based on nanotechnology aims to target the medication payload to the appropriate location and time at the proper (ideal) dosage [39].

- **Targeted Drug Delivery:** The development of targeted drug delivery systems using nanoparticles has recently been reviewed. Active or passive methods might be used to carry out targeted delivery. To be delivered to a tissue or cell-specific ligand via conjugation, medication or another delivery technique, the therapeutic agent must be actively targeted. Targeting can be done passively by encapsulating the drug in a macromolecule or by having a nanoparticle passively travel to the target organ. The enhanced permeability and retention (EPR) effect can be used to passively target drugs or medications encapsulated in nanoparticles and linked to macromolecules [32].

- **Stimuli-Responsive Systems:** Nanoscale drug delivery techniques that react to particular stimuli like temperature, pH, light or enzymes are being developed by scientists. In reaction to the unique circumstances, these systems can be created at the intended location to release medications under regulated settings. The potential for on-demand drug release and improved treatment efficacy is provided by stimuli-responsive devices. Nanoscale stimulus-responsive devices might be sensitive to particular endogenous stimuli, including reduced interstitial pH, increased glutathione levels or elevated levels of specific enzymes like matrix metalloproteinases [40-41].

- **Combination Therapy:** Research is now being done on the use of numerous therapeutic agents in a single nano drug delivery system. Researchers want to improve treatment outcomes and combat drug resistance by combining various medications with complementary mechanisms of action. Utilizing nanoscale drug delivery devices, combination therapy can increase drug synergy, lower systemic toxicity, and enable the sustained release of numerous medications [42-43].

- **Gene Delivery:** Researchers are looking into using nanoparticles as carriers for gene therapy. In order to rectify genetic diseases or modify gene expression for therapeutic purposes, researchers are looking at the transfer of therapeutic genes to target cells using nanoparticles. For effective and targeted gene delivery, strategies including either viral or non-viral vectors are used, such as lipid nanoparticles or polymeric nanoparticles. Although there are several methods for delivering genes, nano-carrier systems appear to be a great choice for effective gene delivery. One of the most crucial aspects in gene therapy is making the right carrier system selection. Numerous nanocarrier systems including polymeric, liposome, dendrimer, metallic, gelatine, quantum dots, protein, graphene nanocarriers, stimuli response nanocarriers, magnetic nanocarriers and protein nanocarriers have been created effectively [44-45].

- **Controlled Release:** Therapeutic drug's release rate and duration are controlled using controlled release systems in an effort to increase their effectiveness and minimize negative effects. Designing nanocarriers that react to multiple stimuli such as pH, temperature, enzymes or light in order to induce medication release at the desired site and time is a current area of research. By lowering the dose and frequency of administration, nanocarriers that can distribute medications in a spatiotemporally

regulated manner may improve therapeutic efficacy, lessen systemic side effects and increase patient adherence to regimens. A variety of nanocarriers with different compositions have been created to attain this purpose, surfaces, morphologies, and characteristics. Nanocarriers are designed to exploit the enhanced permeability and retention (EPR) effect, enabling their targeted accumulation within tumors. This strategy aims to effectively regulate the spatial distribution of medications [46].

- **Immunotherapy Enhancement:** In order to increase the efficacy of immunotherapy, which has demonstrated encouraging outcomes in the management of cancer, researchers are looking into nanoscale drug delivery methods. To enhance immune response and overcome resistance, strategies entail providing immune modulators, such as checkpoint inhibitors or immunostimulatory drugs, directly to the tumor microenvironment. A multitude of preclinical investigations and preliminary clinical findings indicate that the application of nanotechnology has promise in overcoming the existing limitations of cancer immunotherapy. In order to enhance the bioavailability and stability of therapeutic medications, nanoparticles can be employed to facilitate their targeted delivery to specific anatomical sites inside the body. This can be achieved through several means, such as systemic administration, tumor implants, microneedle injection, or the utilization of tumor-homing peptides [47-48].

- **Nanoscale Imaging Agents:** In order to increase diagnostic capabilities, nanoparticle are being investigated as imaging agents. Researchers are currently developing nanoparticles for utilization in imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI), and fluorescence imaging. These imaging tools can help with early illness detection, pinpoint therapy target localization and treatment response tracking. This option is provided via nanoparticle technology. Nanoparticle-based contrast agents are widely employed in a variety of prominent biomedical imaging techniques such as fluorescence imaging, magnetic resonance imaging (MRI), computed tomography (CT), ultrasound (US), positron emission tomography (PET) and single-photon emission computed tomography (SPECT) [49].

- **Biocompatibility and Safety:** Current research focuses on evaluating the biocompatibility and long-term safety profiles of nano drug delivery devices as they get closer to clinical use. In order to ensure the safety of their use, research is being done to assess potential toxicity, immunological responses, and the elimination of nanocarriers from the body [50-51].

- **Theranostic:** Theranostic treatment, which combines therapy with diagnostics, is widely applied to the treatment of cancer. Theranostic nanoparticles may prove useful to identify the place, describe the condition, and stage of the illness, and provide details on the response to treatment. In addition, nanoparticles have the capability to transport a therapeutic medicine that is particular to a tumor, hence facilitating the targeted delivery of the necessary concentrations of the therapeutic agent through external or molecular stimuli [37].

III. TYPES OF NANO-DRUG DELIVERY SYSTEMS

The four main subcategories of nanoparticles are lipid-based, polymeric, nonpolymeric, and nanocrystalline. Micelles, drug conjugates, gels, protein nanoparticles, and dendrimers are a few examples of nanoparticles formed of polymers. Nanodiamonds, silica, quantum dots, carbon nanotubes and metallic nanoparticles are examples of nonpolymeric nanoparticles. Lipid-based nanoparticles include liposomes and solid lipid nanoparticles (SLNs). Crystalline nanoparticles are produced by combining therapeutic substances in the crystal form [52]. These are discussed below:

1. Polymer-Based Nanoparticles: Nanoparticles made of polymers can be created artificially or naturally. In terms of therapeutic applications, they provide an alternate strategy emphasizing biocompatibility, no immunogenicity, nontoxicity, and biodegradability [52].

- **Dendrimers:** Highly branching macromolecules resembling trees are called dendrimers. They are excellent for targeted medication administration and imaging applications because they can be synthesized with fine control over their size and surface functionalization [53].

- **Micelles:** Amphiphilic molecules create self-assembling micelles in an aquatic environment. They have the ability to solubilize hydrophobic medications inside of them, improving drug delivery to targeted areas [54].

- **Drug Conjugates:** Low-solubility medicinal drugs are most frequently delivered by means of micellar solutions. Micelles collect in the solvent and have a diameter of around 100 m. In a spherical form, the molecules that make up polymeric micelles are organized, with a mantle of the hydrophobic centers surrounded by hydrophilic groups. The great stability of the hydrophilic surface inside physiological systems provides defense against nonspecific absorption by the reticuloendothelial system [52].

- **Protein Nanoparticles:** These nanoparticles have good biocompatibility and the possibility for tailored administration since they use proteins or peptides as carriers [55].

- **Nanogels:** Colloidal or polymeric gels are characterized by their nonfluid nature, forming networks that undergo expansion upon interaction with a fluid medium. According to the International Union for Pure and Applied Chemistry (IUPAC), nanogels are gel particles that possess the following attributes: a diameter of less than 100 nm. The capabilities of swelling nanogels are made of naturally occurring or manufactured polymers that have been mechanically or chemically crosslinked, resulting in their flexible scale and high-water concentration [56].

2. Lipid-Based Nanoparticles

- **Liposomes:** Amphiphilic phospholipids are used to create synthetic liposomes, which self-assemble. They consist of spherical double-layered vesicles that can be as small as 50 nm around an aqueous core domain. General Biological properties of liposomes that are appealing include biocompatibility and biodegradability. Liposomes are widely utilized in clinical studies as medication delivery methods [54].

- **Exosomes:** Exosomes are diminutive extracellular vesicles that play a crucial role in facilitating the transportation of various biomolecules and mediating intercellular communication. Most cell types, including different kinds of body cells like immune cells, stem cells, and cancer cells, release them. They are a sort of nanoscale vesicle that ranges in diameter from 30 to 150 nanometers. Exosomes have garnered significant interest in the field of biomedical research and medication delivery owing to their participation in a diverse range of physiological and pathological mechanisms [57].

- **Solid Lipid Nanoparticles:** Solid lipid nanoparticles (SLN) were developed as a controlled substitute for emulsions, liposomes, and protein nanoparticles (PNPs) in the context of a colloidal drug delivery system. Solid lipids are employed in the production of solid lipid nanoparticles (SLNs), which are subsequently stabilized through the incorporation of one or more surfactants. The use of SLN presents several advantages over alternative approaches for medicine delivery. The ocular route offers notable advantages in terms of superior tolerability, biodegradability, high bioavailability, and the ability of particle

carriers to exert specialized effects on the brain [54].

3. Nonpolymeric Nanoparticles:

- **Carbon Nanotubes:** The identification of carbon nanotubes may be traced back to the year 1991. These structures are composed of carbon and take the form of tubular shapes. The tubes are comprised of graphite sheet cylinders that have been securely sealed. The buckyballs exhibit the presence of functional groups at either one or both termini, while their length spans a range of 1 to 100 nanometers. In recent times, there has been a surge in the popularity of single-walled nanotubes (SWNTs) and two distinct categories of multi-walled nanotubes (MWNTs). Additionally, it is worth noting that MWNTs are commonly seen in conjunction with C60-fullerenes. They arrive in several graphite cylinder arrangements and are hollow and noted for resembling cages and nanotube fullerenes. They are appropriate for encapsulating drugs due to their size and external characteristics and they have essential physical attributes [58, 52].

- **Nanodiamonds:** Typically, the size of nanodiamonds (NDs), which are carbon nanoparticles characterized by a truncated octahedral structure, falls within the range of 2 to 8 nm. Nanomaterials possess several advantageous characteristics, including their diminutive size, expansive surface areas, chemical stability, and exceptional hardness, stiffness, and strength. Moreover, they demonstrate numerous superior attributes akin to diamond, such as a high capacity for adsorption and a substantial surface area. Therefore, the physical and chemical characteristics of NDs are superior over customary materials [50].

- **Metallic Nanoparticles:** Metallic nanoparticles are made up of metal atoms. Nanoparticles generally exhibit dimensions ranging from 1 to 100 nanometers. They differ from their bulk counterparts in that they have special size-dependent features. These characteristics make them appealing for a variety of applications in numerous disciplines, such as environmental science, materials science, electronics, catalysis, and medicine [58].

- **Quantum Dots:** Quantum dots (QDs) consist of semiconducting structures ranging in size from 2 to 10 nm. They are zinc sulfide-coated organic nanocrystals with a CdSe (Cadmiun selenide) inorganic semiconductor core that are intended to glow under certain lighting conditions and it is of light's influencing nature. The inclusion of a cap enhances QDs' ability to dissolve in aqueous buffers [58].

- **Silica-Based Nanoparticles:** Silica-based nanoparticles possess notable advantages in the field of nanomedicine, mostly attributable to their affordability and versatility in simulating intricate systems. Due to some certain surface characteristics, porosity, and functionalization, they are attractive therapeutic delivery methods where polar silanol units shield the silica nanoparticles' large surface area, making them water- friendly. They increase medicinal agent's adsorption and also their stability [59].

4. Nanocrystalline: A substance or material that is "nanocrystalline" is made up of grains or crystals that are smaller than a nanometer. Crystalline materials feature distinct crystalline areas with a distinctive lattice arrangement, and their atomic structure is regular and recurring. These crystallites have special characteristics that set them apart from their bulk counterparts when they are shrunk to nanoscale dimensions. Frequently, the grain sizes typically span from a few nanometers to several hundred nanometers. Due to their improved mechanical, electrical, magnetic, and optical capabilities, nanocrystalline materials have attracted substantial attention in a number of sectors [60- 61].

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IV. CONCLUSION

Nano-drug delivery systems have emerged as a transformative approach to significantly enhance the bioavailability and bioactivity of various therapeutic agents. This chapter has provided a comprehensive overview of the diverse nano-based technologies utilized for targeted drug delivery, controlled release, and improved therapeutic efficacy. Through the ingenious use of nanoparticles, such as liposomes, polymeric nanoparticles, dendrimers, carbon nanotubes, metallic nanoparticles, solid lipid nanoparticles, and protein-based nanoparticles, researchers have unlocked new avenues to address the limitations of conventional drug delivery methods. By encapsulating drugs within these nanocarriers, it has become possible to protect

sensitive drugs from degradation, extend their circulation time, and overcome biological barriers to enable selective targeting of diseased tissues or cells. The ability to achieve sustained and controlled release of drugs from nano-carriers allows for reduced dosing frequency, minimizing adverse effects, and increasing patient compliance. Moreover, the surface functionalization of nanoparticles enables specific ligand-receptor interactions, directing drugs precisely to their intended sites of action, thus optimizing therapeutic outcomes. The potential of nano-drug delivery systems extends beyond their ability to improve drug bioavailability and bioactivity. These platforms have shown promise in combination therapy, co-delivery of multiple drugs, and integration with diagnostic imaging agents, paving the way for personalized medicine and more effective treatment strategies.

As research in the field continues to advance, challenges related to large-scale production, regulatory considerations, and long-term safety profiles must be addressed to accelerate the translation of these technologies from the laboratory to clinical practice. Nevertheless, the progress achieved thus far in nano-drug delivery systems offers a glimpse into the future of pharmaceutical sciences, with the potential to revolutionize the treatment landscape and improve patient outcomes across a wide range of medical conditions. Embracing the promise of nano-based drug delivery represents a promising pathway toward the realization of safer, more efficient, and patient-tailored therapies in modern medicine.

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