

Original Article: Synthesis and Characterization of Novel Nanomaterials for Drug Delivery Applications

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Citation N Bahadori., *Synthesis and Characterization of Novel Nanomaterials for Drug Delivery Applications*, EJCMPR. 2024; 3(4): 1205-1220

 <https://doi.org/EJCMPR/4222516>

Article info:

Received: 01 August 2024

Accepted: 01 October 2024

Available Online:

ID: EJCMPR-2410-1220

Checked for Plagiarism: Yes

Peer Reviewers Approved by:

Dr. Frank Rebout

Editor who Approved Publication:

Dr. Frank Rebout

Keywords:

Nano medicine, patient, injection method, synthesis of drug carriers, micro particles.

ABSTRACT

Nano systems synthesized from organic and inorganic materials have attracted a lot of attention for biomedical applications. These applications can be in the fields of biosensors, manufacturing imaging systems, synthesis of drug carriers and targeted drug delivery. The use of particles for drug delivery was first popularized by using diagnostic drugs in reticuloendothelial systems (liver, spleen, bone marrow, and lymph nodes) and caused the increasing expansion of micro particle systems. Increasing the dissolution of drugs by reducing the particle size is one of the most important goals of using these particles. However, the use of micro particles has many other advantages. The results of the present study showed that by reducing the particle size of drugs, their shelf life in the body is increased. Because the particles are less accessible to the elimination systems of the body, such as kidney, liver, etc., and as a result, the possibility of removing them from the body decreases. For this reason, the shelf life of medicines in the body increases and the number of times the medicine is used decreases. Also, with this method, in addition to the lower cost that the patient pays due to reducing the frequency of drug use, the side effects of the drug also appear less in the patient. Consuming regimens lead to more patients. Over many years, the use of micro particles became very popular and was able to make valuable progress in the field of drug therapy, but micro-scale materials often show the same physical characteristics as bulk and macromolecules. In addition, the results showed that for more access to the cells and drug delivery to them, the drug carrier should be in the dimensions of the cells themselves and their internal organs.

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Introduction

A After a decade of research and development, nanotechnology was able to change the traditional way of using ceramics in drug delivery. Although polymers have dominated drug delivery, now it is the use of ceramics that has created great hopes in drug delivery. Nanotechnology is the science of using materials and systems that, when they reach Nano dimensions ($>100\text{nm}$), their structure and components show new and extensive changed properties. Nowadays, drug delivery is one of the fast and advanced phenomena for Nano ceramics, which has attracted a lot of attention. The extraordinary characteristics of Nano ceramics, including size, structural pores, highly active surfaces, unique chemical and physical properties, and ease of modification show that, compared to polymeric species, Nano ceramics are an excellent vehicle for controlled and long-term drug delivery and release. Advanced Nano ceramics used in drug delivery systems give the hope of being able to solve many challenging medical problems.

Classification of Nano ceramics

1- Ceramic nanoparticles: Ceramic nanoparticles are special drug carriers that have various benefits for use in drug delivery systems, and today they are considered ceramic drug delivery systems. These carriers, just like their polymer counterparts, transport the drug in ways with limited volume such as blood vessels, the digestive tract, and the width of biological membranes and deliver it in a minimally invasive manner. Also, Nano ceramic carriers have a high surface-to-volume ratio, which enables the loading of a large amount of drug and long-term drug release. Also, these materials are easy to make and cheap to produce. Advances in nanotechnology have resulted in the production of very small particles with high purity and with a very high

surface-to-volume ratio, making it possible to manufacture with great control over particle size, morphology, and pores. Nanoparticles carrying drugs increase endocytosis of drugs by target cells and facilitate deeper penetration into capillaries and membranes in order to increase absorption. For example, nanoparticles with dimensions of $10\text{-}70\text{ nm}$ can penetrate capillaries and nanoparticles with size of $70\text{-}200\text{ nm}$ will have the longest circulation compared to other sizes. The high surface-to-volume ratio of nanoparticles and their high surface activity increase the efficiency of nanoparticles in drug loading and stability.

A) The superiority of ceramic nanoparticles over polymers in drug delivery: almost all the benefits mentioned for nanoparticles also apply to polymers. So how do ceramic nanoparticles outperform polymers in drug delivery? Compared to polymers or metal nanoparticles, ceramic nanoparticles have several unique properties. The biodegradability period of ceramic nanoparticles is usually long. A characteristic that seems to be critical in the speed of permeation and the control of drug release. The slow degradability or even the indestructibility of ceramic matrices can keep drugs for a long time after application, and in this case, the long-term release of the drug will depend on the concentration gradient. Unlike polymers, ceramic nanoparticles do not swell in water, or change in porosity, and remain highly stable when changes in pH or temperature occur. For example, a problem that usually occurs in hydrogel drug delivery systems is the explosive release of drugs, which is prevented by small swelling ratios in ceramics. The fabricated ceramic nanoparticles can have the same chemistry, crystal structure and size as the constituents of target tissues.

B) Controlled drug release: drug delivery models can be divided into continuous or

discontinuous (on-off) models. In each model, nanotechnology is used to control drug delivery. For example, in cases such as treating diabetes or suppressing post-operative inflammation, medical researchers prefer a continuous but time-delayed drug delivery model with sustained release over the initial burst release of the drug. Conversely, for discontinuous delivery, such as timed drug delivery to cancer cells or pathogen sites, burst drug release is often more desirable. In the next step, researchers target the drug to specific areas such as pathogens, tissues or cells. Targeting, because it increases drug efficiency and reduces side effects such as toxicity, is very desirable and challenging. However, ceramic nanoparticles have significant potential in facing challenges due to their unique properties.

2- Calcium phosphate: Calcium phosphate is an example of Nano ceramics that has been widely studied due to its biocompatibility, absorption and suitable biological activity. Calcium phosphate has been used as a new delivery carrier for antibiotics (gentamicin sulfate, tetracycline), anti-inflammatory agents (such as salicylic acid), painkillers and anticancer drugs (such as mercaptopuril), growth factors, and genes. Calcium phosphate Nano derivatives successfully perform sustained and continuous release over time. Investigations show that the speed of drug release can be proportional to the granulation size of calcium phosphate nanoparticles, the surface area and the ratio of calcium to phosphate. Researchers have designed and manufactured calcium phosphate nanoparticles that deliver drugs in a programmed on-off manner by external forces such as ultrasonic vibrations with a certain amount of power.

Interstitial ceramic nanostructures

All interstitial nanostructures made of ceramic materials have one thing in general, and that is the infinitely high ability to load the drug along with its delayed release compared to bulky Nano spheres. For example, studies show that inter-zero silica Nano spheres have the ability to trap eight times more medicinal species compared to solid silica Nano spheres. Also, the mid-null silica Nano ambassadors have a multi-stage delayed release profile that includes an initial burst release for 20 minutes, a long-term sustained release of over 10 hours, and a rapid final release for another 2 hours. Targeted drug delivery is investigated by biochemically modifying drug carriers that specifically bind to target cells, or by using external devices that cause the drug carrier to move to the affected areas. Recently, two emerging topics for the use of ceramic nanoparticles in drug delivery have received attention. One is photodynamic therapy (PDT) and the other is layered double hydroxides (LDHs). PDT is a method for treating various diseases such as glandular, heart, skin and eye diseases. PDT is the absorption of light-sensitive materials (silica) by diagnostic tissues (cancerous tissues) after photo irradiation. LDHs belong to a class of ceramic materials with anionic layers, which are composed of charged metal hydroxide layers and anionic regulating complexes. Metal cations in LDH include: Mg^{2+} , Zn^{2+} , Ni^{2+} , Cu^{2+} , Al^3 and Fe^{3+} , and interlayer anions can be $-CO_3^{2-}$, NO_3 and $-SO_4^{2-}$. LDHs are bio absorbable and have high ion exchange capacity, high growth and pH-dependent solubility. These properties of LDH show promise for drug and gene delivery. LDHs are made by adding a strong base solution to a solution containing metal cations, and their size is easily controlled by pH, temperature, and reaction time. The LDH-bound anticancer drug methotrexate has much greater anticancer activity in vitro than the clinically used doxorubicin. This is believed

to be due to high cellular uptake of the drug through clathrin-dependent endocytosis and controlled intracellular release. Recent studies

show that LDHs with dimensions of 200-100 nm may have better drug delivery and less toxicity (Figure 1).

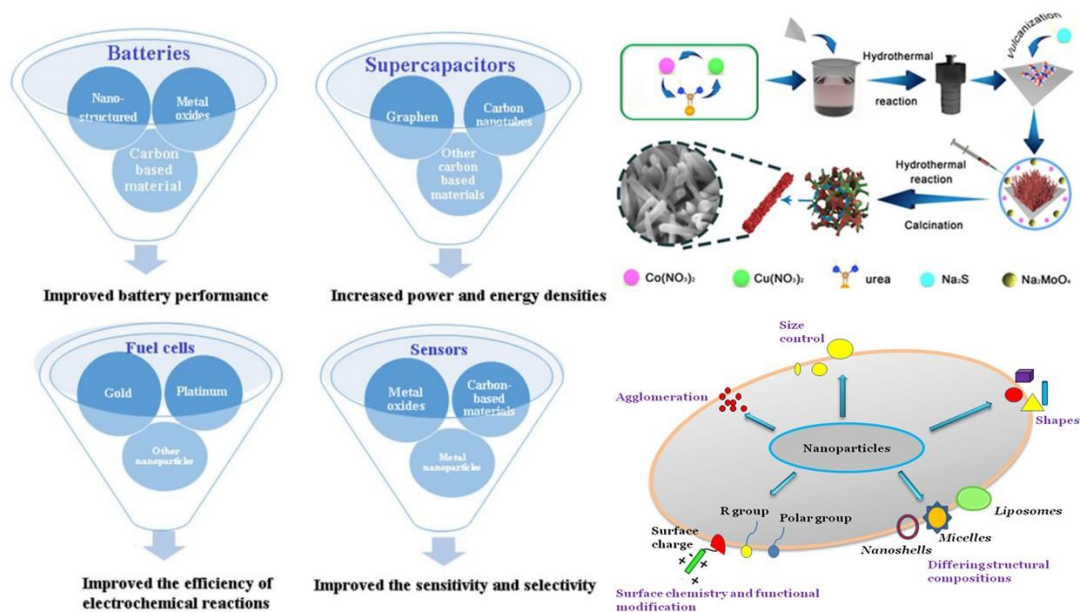


Figure 1. Synthesis and Characterization of Novel Nanomaterials for Drug Delivery Applications

Ceramic Nano scaffolds for drug delivery and tissue regeneration

Ceramic scaffolds, similar to their nanoparticle counterparts, have great potential in controlled drug delivery. At first, these scaffolds were imitated and designed as protective structures to control and direct cell behaviors by the environment. Examples are calcium phosphate scaffolds that mimic the structure and chemical composition of natural bone. Calcium phosphate scaffolds not only provide primary structural strength for bone cells, but also promote proliferation and differentiation and can aid in the eventual accumulation of new tissue. Such scaffolds simulate the environment inside the body of cells more completely than nanoparticles. Therefore, the development of biomimetic Nano scaffolds seems to be an essential need. Bone in nano dimensions is a combination of collagen fibers and calcium phosphate crystals, both of which are Nano components. The structural benefits of ceramic Nano scaffolds include: large pores, high

volume-to-surface ratio, large surface area, high structural stability, and long degradation time. These features make them a powerful system for in-situ drug storage and release for antiseptic and anti-inflammatory purposes. Therefore, most ceramic Nano scaffolds are considered multifunctional pharmaceutical systems (drug delivery, cell growth guidance or tissue production and mechanical protection). Hence, the mechanical protection provided by ceramic scaffolds is more than expected by polymer scaffolds.

Nano particles and drug delivery through the skin

In order to improve the delivery of drugs through the skin, various chemical and physical technologies have been developed. An example of these technologies is the use of nanoparticles in drug delivery. In order to optimize drug delivery, one should first get acquainted with the physiology of the skin and use the methods that are suitable for the cells of this structure

spread over the body. Due to the very small size of the ways of entering the compounds into the skin (less than 10 nm), for the preparation of nanoparticle formulations, compounds that can help enter the substances into the deeper layers of the skin should be used. Compounds such as surfactants in the formulation of nanoparticles are known as a factor for optimizing the absorption of substances through the skin. This is the reason why surfactants have been used in the construction of most of the nanoparticles that can be used locally.

Synthesis methods of titanium dioxide nanoparticles and its application in drug delivery to wound dressings

Metal nanoparticles and metal oxides, including titanium dioxide nanoparticles among polymeric nanoparticles, liposomes, micelles, quantum dots, quantum dots, dendrimers or fullerenes, have become increasingly important due to their potential use in new medical treatments. In recent advances in the synthesis of titanium dioxide nanomaterials, which include the synthesis of titanium dioxide nanoparticles, Nano rods, nanowires, nanotubes and mesoporous or Nano porous materials using different preparation methods such as sol-gel, sol, hydrothermal, solvent Heat and vapor deposition, which are the most used in sol-gel synthesis and hydrothermal methods, and green chemistry and microwave methods are also increasing, as well as the use of titanium dioxide nanoparticles along with antibiotics, growth factors, and polymers, including Polysaccharides and other nanomaterials are used by researchers today in drug delivery to wound dressings, especially in the form of nanofibers or hydrogels in diabetic wound models. One of the most widely used nanomaterials used in Nano medicine is polymer nanoparticles (NPs). These types of

nanoparticles, having diverse properties, draw a step towards a bright future for improving the quality of treatment using modern Nano medicine methods. In recent years, researchers have investigated and scientifically studied various factors such as particle size, morphology of polymer nanoparticles, selection of material type and synthesis techniques and optimization of nanomaterials in order to provide an ideal Nano system for targeted and more effective drug delivery. Polymeric nanoparticles are used in various therapeutic techniques such as targeted drug release, vaccines, tissue engineering, and various imaging methods. Scientific research at the frontier of knowledge regarding the use of polymer nanoparticles in the field of cancer, neurogenic disorders and cardiovascular diseases is being carried out at the international level. Cells exhibit diverse responses at the nanoscale level. Understanding the interaction of nanomaterials and biological compounds and Nano biotechnological studies is very necessary and important. In order to understand different dimensions in this field, researchers need to conduct experiments such as investigating the properties of nanomaterials and biological compounds, analyzing the kinetics of mass transfer, the duration and method of cleansing from blood, changes in gene expression, effects on chemical structure, surface charge, and signaling. do biomolecular and toxicity. In order to study this type of interactions in terms of the toxicity of nanomaterials, there is a need to design a set of control experiments. Based on Duncan and Vincent's research, polymer therapies include: polymer drugs, polymers functionalized with proteins and drugs, copolymer micelles with covalent bonds, and multiple viral and non-viral vectors. Polymers have found wide applications in therapeutic programs due to the diversity in different methods of

functionalization, diverse methods of macromolecular synthesis and polymer diversity. The first category of polymer nanoparticles used in Nano medicine were non-biodegradable nanoparticles such as polymethacrylic methacrylate (PMMA), polyacrylamide, polystyrene and polyacrylates. Release systems based on non-biodegradable nanoparticles were designed to be quickly and effectively removed from the bloodstream through feces or urine. Because these type of polymer nanoparticles are not easily decomposed and their accumulation in body tissues causes toxicity. Non-biodegradable polymer particles are used in various aspects of Nano medicine, including targeted drug release, wound healing dressings, and antimicrobial medical coatings. Chronic poisoning and inflammatory reactions are among the side effects of using non-biodegradable materials. These side effects have led to the start of research on alternative options such as biocompatible materials with degradability. Biocompatible polymer materials were proposed as a suitable alternative to non-biodegradable polymer materials in the field of Nano medicine due to their lower toxicity and ability to create a specific drug release pattern and increase biocompatibility. Biodegradable polymers are:

1- Kinetic polymers: Kinetic polymers such as poly (lactide) (PLA), poly (lactide glycolide) copolymers (PLGA), PCL polycarbonate) and poly (amino acids).

2- Natural polymers: natural polymers such as chitosan, alginate, gelatin and albumin.

Among the characteristics of nanomaterials used in Nano medicine, we can mention increasing the permeability of cells, increasing the efficiency of targeted drug release, reducing the amount of dosage and frequency of use, and improving the effectiveness of medicinal agents. In addition, nanotechnology provides

the ability to combine multiple therapeutic agents, control and targeted drug release. By summarizing the research results on the relationships between the physical and chemical properties of nanomaterials and the biological functions of the surrounding environment, the high potential of polymeric nanoparticles can be better understood.

Corona protein

When a biological system is exposed to nanoparticles, a series of protein-nanoparticle interactions take place and cellular uptake occurs. The surface of nanoparticles can play the role of a scaffold for the binding of ligands or proteins, which finally ends in the formation of what is called the corona of protein nanoparticles.

Nell et al describe Nano bio interaction as dynamic physical and chemical interactions, kinetics and thermodynamic exchanges between nanomaterial surfaces and biological fluid surfaces. This protein layer around the nanoparticles acts as a biological identity that is the main responsible for the interaction with living cells. Unfortunately, there is little information about the corona protein and the proteins involved in its formation. Cell uptake probably causes changes in the conformation of proteins, membrane interactions, transfer phenomenon, aggregation and signaling in cells. Corona protein leads to changes in surface properties, basically a new substance with different biological properties is created according to the absorbed proteins. The mechanism of the corona protein is not fully known and it cannot be definitively stated that when the nanoparticle reaches the cell, the corona protein changes, or the structure and conformation of the proteins undergo changes, or the cell membrane is affected, or some other unknown phenomenon. The size of the particles can be affected by several different factors such as the type of polymer, surfactant

and concentration and different parameters of the synthesis method such as the type of method, nozzle diameter, flow rate, selected initiator, selected monomer, polymerization and type of emulsion. According to the conducted research, the signaling process and the extracellular transfer process take place at the Nano scale. In addition, release efficiency, targeting, degradation and degradation rates, toxicity, respiration, and cellular uptake mechanisms are all directly related to particle size.

Cell membrane interactions with nanoparticles have an effect on the absorption of nanoparticles by the cell and are defined in two consecutive stages: in the first stage, the process of connecting the particle to the cell membrane and in the second stage, intracellular processes take place. The size of nanoparticles significantly affects the binding process and intracellular interactions. In the scientific research that was done earlier by Wen and Feng to analyze the size and surface coating of polymer nanoparticles (such as polyvinyl alcohol and vitamin E TPGS) on the absorption efficiency of cells for chemotherapy for oral drugs, the effective size of nanoparticles for absorption by cells Caco-2 (clonal carcinoma cell line) was reported to be between 100 and 200 nm. Smaller nanoparticles usually have a higher cellular absorption efficiency, and the size of 50 nm is defined as the threshold of cellular absorption. Recently, Hay et al. investigated the effects of changes in the size and surface charge of polymeric nanoparticles on the uptake by cancer cells simultaneously. The polymerization of methyl methacrylate with chitosan derivatives was carried out by these scientists to determine the effects of cell absorption on phagocytic and non-phagocytic cells and to investigate their biological distribution. For macrophages, these researchers concluded that high surface charge

has a significant effect on cellular uptake of larger nanoparticles. Because in the case of cellular absorption of larger polymer nanoparticles by non-phagocytic cells, more energy is required and as the size of the nanoparticle increases, the amount of cellular absorption also decreases. The cut-off for the absorption of nanoparticles by the non-specific endocytosis mechanism for polymer nanoparticles has been determined to be 150 nm.

Kankarlı and Feng investigated the size of polystyrene nanoparticles in the size range of 25 to 500 nm for drug delivery and crossing the blood-brain barrier (BBB). Nanoparticles smaller than 200 nm are absorbed by Caco2 and Madin-Darby cell lines. The highest absorption efficiency was reported for nanoparticles with a size of 100 nm, and nanoparticles with a size of 500 nm were absorbed with a very low percentage. Nanoparticles smaller than 100 nm are cleared by the (RES) system, which reduces the efficiency of cellular absorption and reduces the duration of retention in the blood circulation. In addition, smaller nanoparticles have lower surface energy and do not provide the minimum energy required for binding and the endocytosis process. The type of cellular uptake process is directly related to the size of the nanoparticles. Published articles by various researchers suggest that smaller nanoparticles are absorbed using cellular receptors and larger nanoparticles are absorbed by the phagocytosis mechanism. Among the various scientific papers that have been reported so far, the ideal size of nanoparticles has been reported in very different amounts. Various researches on several scientific reports have presented conflicting results based on the type of cell selected, properties of nanoparticles and surface properties, different values of dispersion index, etc. Finding a suitable solution to the challenge of proper size of

nanoparticles is very difficult due to the complexities of Nano biological interaction. Therefore, it is difficult to determine the optimal size of nanoparticles for specific applications.

Particle geometry

The shape and morphology of nanoparticles has a significant effect on the absorption and transport of nanoparticles in the physiological system. Most of the research has been done on spherical nanoparticles due to their many advantages. These benefits are classified into four categories:

- ❖ Changeable and flexible platform for synthesis.
- ❖ High surface to volume ratio.
- ❖ Shape and size.
- ❖ Unique optical properties.

These properties are considered ideal in adopting appropriate strategies for the development and design of therapeutic Nano systems. Also, in Nano medicine, asymmetric and non-spherical polymer nanostructures are used as a solution to overcome the challenges of complex biological systems. Adjusting the geometric properties of nanoparticles allows changing the physical and chemical properties of nanoparticles. Nanoparticles with anisotropic shape have exclusive interactions with the physiological system, and in terms of adhesion, transport, targeted drug release, circulation time and mobility, the anisotropic shape of nanoparticles has many advantages for various Nano medicine applications. Among these applications, we can mention the use of sensors in Nano biology, self-assembly, tissue engineering, immune system engineering, and targeted drug release.

In a review article published by Tao et al., they investigated various Nano morphologies created based on different top-down manufacturing methods, such as molecular molding methods, polystyrene particle

stretching, S-step lithography of polyethylene glycol acrylate, and electromagnetic electronic printing. has been paid This unique morphology creates complex surfaces that enable greater control over targeted delivery based on the increased loading potential of various ligands on the Nano system surface. However, it is very difficult to understand the surface interactions of cells and how anisotropic nanoparticles interact with cells. Because it is possible for a particle to be transferred with different states of the cell. For example, a multifaceted particle can interact with a cell from many different faces of different sizes, and this in turn causes different cellular responses.

In a study conducted by Gratton et al., hydrogel particles with micrometer dimensions were made in different shapes. The effect of the morphology of these nanoparticles on endocytosis and migration on the human cervical carcinoma epithelial cell line (HeLa) was investigated. The results of this research showed that the rate of cellular absorption of anisotropic nanoparticles is faster and higher than symmetric nanoparticles.

Also, in another study conducted by Mitaguchi et al., particles with a higher length-to-width ratio were considered to inhibit phagocytic activity. The results of this research showed that the particles with less curvature lowers the binding potential of the ligand to the nanoparticle and the same thing causes a decrease in phagocytic activity. These results provide useful information for the design of targeted drug release systems in the future. The research carried out so far suggests that there is an optimal and ideal geometry and size for each application, especially polymer nanoparticles in various aspects of Nano medicine.

Challenges of nanoparticles

Despite the advantages of using polymer nanoparticles for various therapeutic applications, such as the development of smart treatments or personalized medicine, one of the limitations of this method is the small number of nanoparticle-based products approved by the FDA. Research in the field of Nano medicine is very extensive and there is a need for additional studies to understand complex areas such as toxicity, bio distribution, biodegradability, human clinical evaluation and appropriate characterization methods.

Sustainability

Nanoparticle formulation stability and structural integrity and chemical composition influence the toxicity and bio distribution of nanoparticles throughout the body. Lazzari et al. used DLS and spectrophotofluorimetric techniques to detect and evaluate the accumulation of nanoparticles in vivo. Researchers treat the surface of the particles with different coatings for the chemical changes of the surface and ultimately the stability of polymer nanoparticles. Drug stability and targeted release is one of the main challenges of nanomaterials used in Nano medicine. Explosive release of materials loaded on nanoparticles has a negative effect on the drug delivery process. Because the gradual release of drugs is one of the basic principles of targeted drug release.

Zhu et al. reported this paradigm by introducing a thermosensitive hydrogel with burst release of doxorubicin (DOX) hydrochloride and slow release of paclitaxel (PTX) for antitumor therapy. The distribution of nanoparticles includes two related challenges in the field of accumulation of nanomaterials in unwanted places and misdiagnosis of the target tissue. Different barriers and obstacles that exist in the body provide the possibility of making such

mistakes. The biological distribution and activity of the particles ultimately affect the corona protein, which is initially formed by the contact of nanomaterials with different biological compounds of the body. Corona protein changes on a molecular scale based on blood circulation time. Therefore, its formation in in vitro conditions and in vivo conditions is different among different species. The properties of different barriers and obstacles in the body can play a decisive role on the accumulation or distribution of nanomaterials, and as a result, the required dose of the drug may not be released.

Barua et al have investigated the properties of the main biological barriers present in the body's defense systems, which include the endothelial barrier, cell barrier, skin and mucosal barriers. The biological environment of the blood-brain barrier and the area of cancer tumors are among the most challenging target tissues for the targeted release of drugs using nanoparticles.

Purification of blood circulation

Surface engineering techniques are used to keep nanoparticles in the blood circulation system. Usually, the removal of nanoparticles from the blood occurs by the reticuloendothelial system (RES). Particles with PEG added to their surface show a higher half-life than non-PEGylated nanoparticles. This significantly increases the probability that the particles will reach the target tissue and effectively improve the treatment.

Polymers in drug delivery

One of the most important biomedical applications of biodegradable polymeric nanomaterials is in the field of drug delivery. Polymeric nanomaterials have several advantages, among which the following can be mentioned:

- ❖ The model presents the controlled release of the matrix structure to a particular tissue part of the body.
- ❖ It covers unstable molecules such as DNA, RNA and proteins and prevents their destruction.
- ❖ Suitable for surface engineering with ligands.
- ❖ It is stable in in vitro and in vivo conditions.

Biodegradable polymer nanoparticles for targeted release

Controlled drug delivery occurs when the desired drug is released from the polymer matrix in a designed manner. In recent years, biodegradable polymers with various morphologies such as nanofibers and nanoparticles have been developed and used for drug delivery.

Conclusion

Currently, various types of polymeric nanoparticles have been used in clinical studies. It is possible to use polymer nanoparticles for drug delivery, imaging, treatment and treatment quality improvement programs. Several biodegradable Nano systems based on nanoparticles were designed, synthesized and investigated to improve and facilitate cancer treatment and imaging. By overcoming the conventional limitations of chemotherapy, this type of Nano systems plays a big role as the next generation of treatment in improving the quality of life of cancer patients. Polymeric micelles are a new tool for loading low water-soluble anticancer drugs that increase the lifetime of molecules and a controlled release profile in vitro and in vivo. Optical contrast agents designed and synthesized based on polymer nanoparticles increase the contrast in many medical imaging methods. These types of polymer nanoparticles provide an opportunity to monitor tumor activity. The use of polymer nanoparticles in

modern medicine and Nano medicine improves and facilitates conventional treatments in order to help people on an individual and global level. Conducting more research on Nano systems designed based on polymer nanoparticles at both pre-clinical and clinical levels will significantly improve the quality of prevention, diagnosis and treatment of incurable diseases. Recently, optical imaging has shown significant growth in the field of molecular imaging due to its non-invasive nature and the development of powerful infrared fluorescence (NIRF) imaging tools. The use of several polymer nanostructures to coat non-invasive optical contrast agents such as (ICG) and (NIRF) for optimal imaging in the human body has been reported. These nanoparticles are able to change the state from off to on by using the photo thermal therapy technique in the target tissue to perform accurate imaging. ICG nanoparticles can be used for photo thermal therapy with NIRF laser beam, which is an effective and efficient agent for cancer diagnosis and treatment. In a study, Kim et al introduced ICG-loaded micelles as a non-invasive imaging method by intravenous injection into rat tumor clone CT-26.174. Encapsulation of ICG into ICG-loaded micelles is more efficient, has more stable fluorescence, and has a longer shelf life. Non-cytotoxic fluorescent dyes can be covalently linked to polymer nanoparticles for optical imaging. In addition to natural dyes, there are several studies in which synthetic polymer nanoparticles such as benzothiazolium propanesulfonate (NPBT), benzoinidolium N-propene sulfonate (NPBI) and scorain have been used. Yang et al optimized biodegradable aliphatic photo luminescent polymers (BPLPs) with tenability in vivo. This fluorescence system can be detected by light emission from blue to NIR (up to 725 nm), which can act as a non-invasive and real-time agent. The cross-linked network of BPLPs is synthesized from

biocompatible monomers including citric acid, aliphatic diols and 20 different types of amino acids through polycondensation.

X-ray tomography

Both forms of nanoparticle encapsulation and covalent crosslinking have been evaluated in vivo in CT imaging. In the case of polymeric nanoparticles, mPEG-poly(lactide cross-linked with poly (iohexol) can be used for imaging in vivo. This type of polymer nanoparticles shows better and longer binding than conventional contrast agents. This tool can provide the possibility of tumor detection for a longer period of time for multiple treatment procedures. In addition, effective and efficient contrast agents via encapsulated covalent bonds have been used for CT imaging. For example, Dorais et al tested a stabilized polymer block emulsion to improve the efficacy of an optical contrast agent. This Nano system was made of three hydrophobic polymers in combination with different surfactants and the results show that PBD-PEO is a suitable candidate for use as a blood contrast agent.

PET scan

PET is a nuclear imaging machine that detects small amounts of radioactivity that enter organs and tissues. This technique is known as an applied imaging technique for physiological processes or pathophysiology. Recently, researchers have introduced several contrast agents based on polymer nanoparticles. The choice of contrast agent is determined by the required circulation time. A radioisotope with a longer half-life is required to measure a long time course of circulating nanoparticles after injection. Metal nanoparticles and metal oxides, including titanium dioxide nanoparticles among polymer nanoparticles, liposomes, micelles, quantum dots, dendrimers or fullerenes, have become increasingly important due to their potential use in new

medical treatments. The successful preparation of monodispersed titanium dioxide nanomaterials is the first step towards the realization of the benefits of nanomaterials, and according to the study of numerous articles, using these nanoparticles in wound dressings, we can obtain extremely high antibacterial and antifungal properties. In this review article, finally, according to our own work in the laboratory, the SEM image of polycaprolactone electro spun nanofibers along with titanium dioxide is obtained. The average diameter of Nano fibers is about 123 ± 232 nm and almost without willow, which can be a suitable wound dressing. Cerium nanoparticles can be used in other fields in the future. Cerium oxide nanoparticles are synthesized in different ways in the world, one of these methods is the synthesis of these particles based on the principles of green chemistry. In the usual and conventional methods for the production of cerium oxide nanoparticles, different amino acids and proteins are used as agents that control the dimensions of these particles and stabilize them.

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