Inorganic Nanomaterials for Biomedical Applications

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مستخلص

عندما يتعلق الأمر بتوصيل الأدوية إلى خلايا أو أنسجة محددة، فإن تطوير مواد نانوية غير عضوية مبتكرة تتسم بالتوافق الحيوي، مثل الليبوزومات وجزيئات السيليكا المسامية، يعد أمرًا ضروريًا للغاية. من خلال التنظيم الدقيق لديناميات إطلاق الأدوية وامتصاصها الخلوي، يهدف هذا العمل إلى تعزيز فعالية العلاج مع تقليل حدوث الآثار الجانبية غير المرغوب فيها. من خلال تحسين هذه الخصائص، نرغب في تحسين دقة وكفاءة التطبيقات البيولوجية.

تهدف هذه الدراسة إلى استكشاف التطورات الحالية في استخدام الجسيمات النانوية غير العضوية في الطب الحيوي، مع التركيز بشكل خاص على التطبيقات المحتملة لهذه المواد والآثار التي قد تترتب عليها لأساليب العلاج المستقبلية. خلال إجراء تحليل شامل، نخطط لتقديم رؤى حول الطرق التي يمكن أن تغير بها هذه الجسيمات النانوية أنظمة توصيل الأدوية وتحسين نتائج المرضى.

الغرض من هذه المراجعة هو تسليط الضوء على خصائص الجسيمات النانوية غير العضوية المستخدمة في التطبيقات الطبية الحيوية.

الكلمات المفتاحية: المواد النانوية غير العضوية، التطبيقات الطبية الحيوية، النقاط الكمومية.

Abstract

When it comes to the delivery of medication to specific cells or tissues, the development of novel inorganic nanomaterials that are biocompatible, such as liposomes and mesoporous silica nanoparticles, is absolutely necessary. In the course of doing a comprehensive analysis, we plan to provide insights into the ways in which these nanoparticles have the potential to change medicine delivery systems and improve patient outcomes. The purpose of this review is to shed light

on the properties of inorganic nanoparticles that are utilized in biomedical applications.

Keywords: Inorganic nanomaterials, Biomedical applications, Drug delivery

I. Introduction

The use of nanoscience to create biomedical instruments to accomplish the sophisticated processes of molecular diagnosis, gene/drug delivery/discovery systems, and bioimaging techniques is known as nanomedicine (Park et al., 2020).

Nanopores, nanospheres, nanoclusters, hollow spheres, yolk shells, nanorods, nanotubes, nanowires, core-shell, and other morphologies have been produced at the nanoscale using a variety of nanostructures with varying sizes, shapes, and physicochemical characteristics (Wang et al., 2021).

Metals, metal oxides, alloys, carbon, and other organic compounds can all be used to create these nanostructures. The most often used forms of these nanomaterials in the field of nanomedicine include silicon nanoparticles (SNPs), gold nanoparticles (GNPs), quantum dots (QDs), carbon-based, and biopolymeric nanostructures (Beyene et al., 2021).

II. Inorganic nanoparticles

High-quality nanoparticles with a variety of chemical compositions, including semiconductors, metals, metal oxides, and silica, have been produced via recent developments in colloidal synthesis. These nanoparticles' unique characteristics open up new possibilities for targeted medication delivery and biosensing (Wang et al., 2021).

The most recent advancements in this field of study. the new uses of biological tests based on gold nanoparticles that depend on variations in a colloidal gold solution's visual signature. the uses of the aggregation of noble metal nanoparticles as optical markers in biological research, and the latest uses of nanoparticles in stem cell studies (Hu et al., 2022).

Finally, the paper discusses the advancements in the use of multimodal / multifunctional nanoparticles based on silica for biosensing and bioimaging applications (Zhao et al., 2021) .

Because of the quantum confinement effect, semiconductor nanoparticles—also referred to as colloidal quantum dots—display size-tunable optical characteristics. These quantum dots' chemical makeup consists of II–VI, III–V, and IV–VI semiconductors. (Cho et al., 2024)

They have a continuous excitation band and a narrow emission band, making them stable fluorescence emitters. These quantum dots fall into the UV to near-IR spectral region. Furthermore, when compared to organic dyes, these quantum dots can exhibit orders of magnitude greater cross-sections for two-photon excitation and bigger linear absorption cross-sections for excitation. (Lins et al., 2021)

Colloidal quantum dots are very helpful for biological labeling because of their unique optical characteristics. Colloidal quantum dots functionalized with various bioconjugates have been created thus far for use in a variety of fields, including DNA detection, stem-cell tracking, cell labeling. (Bianchi et al., 2022)

Noble-metal nanoparticles, in contrast to quantum dots, have special optical characteristics brought about by surface-plasmon resonance. Because of the high surface-plasmon connection between the nanoparticles, the aggregation of noble-metal nanoparticles causes noticeable changes in their optical characteristics. (Lu et al., 2021)

Surface-enhanced Raman scattering may result from the greatly increased electromagnetic field in the near-field domain surrounding the aggregation of noble-metal nanoparticles. These characteristics have led to the widespread usage of gold nanoparticles in a variety of assay formats for the detection of proteins and DNA. (Pijeira et al., 2022)

Commercial biomedical assays for the ultra-sensitive detection of disease biomarkers have been created using oligonucleotide-functionalized gold nanoparticles. in this special issue how consecutive silver staining can boost the sensitivity of assays based on gold nanoparticles (Murali et al., 2021).

Iron-oxide nanoparticles are one of the metal oxides that are frequently utilized in biological separation and detection. Superparamagnetic characteristics are displayed by tiny iron-oxide nanoparticles. (Jagiełło et al., 2020)

T2-weighted MRI contrast can result from these particles' reduction of the T2 (spin–spin relaxation time) of nearby protons. Crucially, at low concentrations (in the nanomolar range, for example), these superparamagnetic particles can produce MRI contrast. (Fernandes et al., 2020)

As of right now, the US FDA has authorized Feridex (iron-oxide nanoparticles manufactured by Berlex Laboratories, Wayne, NJ, USA) as an MRI contrast agent for the identification of liver lesions. A novel kind of surface-functionalized iron oxide nanoparticle in this special issue shows greater MRI contrast enhancement than Feridex (Burdușel et al., 2022)

For instance, gold nanoparticles are specifically utilized with photothermal agents in cancer therapy and biosensing, whereas silica nanostructures are typically used as a substrate for drug loading. (Solangi et al., 2024)

However, when it comes to fluorescence characteristics, QDs are well-known for their biosensing uses. Magnetic nanoparticles (MNPs) can be used as imaging aids in magnetic resonance imaging (MRI) due to their super paramagnetic properties (Tee et al., 2021)

III. Nonporous silica nanoparticles (NSNs)

Nano-biotechnology has shown a great deal of interest in nonporous silica nanoparticles (NPs), one of the most significant forms of silica nanoparticles. Amine and carboxyl groups readily functionalize the surface silanol groups (-Si-OH), which are always present on the surface of silica nanoparticles. (Cho et al., 2023)

This procedure will produce NSNs with zwitterionic, positive, or negative surface charges. The way that nonporous silica nanoparticles interact with various biomolecules (such as DNA, proteins, and medications) and cells is significantly influenced by their surface charge and surface chemistry (Fan et al., 2022)

Numerous distinct characteristics of NSNs have been documented, including their hydrophobic surface, highly adjustable size and shape, ease of surface functionalization, high mechanical stiffness, and ease of large-scale synthesis. (Zhang et al., 2021)

Furthermore, it has been established that NSNs have a wide range of biological uses in hydrophobic drug delivery systems, gene and small molecule transport methods, and protein encapsulation processes. In situ synthesis techniques can be used to encapsulate various proteins and medications onto NSNs. Myoglobin, cytochrome c, and copper-zinc superoxide dismutase were all encased in clear silica glass without suffering any appreciable structural or functional changes (Akgöl et al., 2021)

IV. Mesoporous silica nanoparticles (MSNs)

A intriguing option for a new medicine delivery mechanism is mesoporous silica nanoparticles. Some of their important characteristics in a variety of nanomedicine applications, especially as nanocarriers for drug delivery systems, are large internal surface area, extremely high pore capacity, controllable morphologies (size and shape), biocompatibility, ease of synthesis, and ease of surface functionalization. (Tang et al., 2022)

One of the amazing features that is employed as a method for creating drug delivery vehicles with mesoporous silica nanoparticles is the triggered release of loaded pharmaceuticals by the grafting of lids. GSH-triggered drug release is a popular stimulation technique that relies on a redox-responsive mechanism. In this approach, intracellular GSH decreases the disulfide bonds between the capping agents and the surface silanol groups of MSNs. (Rahman et al., 2022)

V. Gold nanoparticles

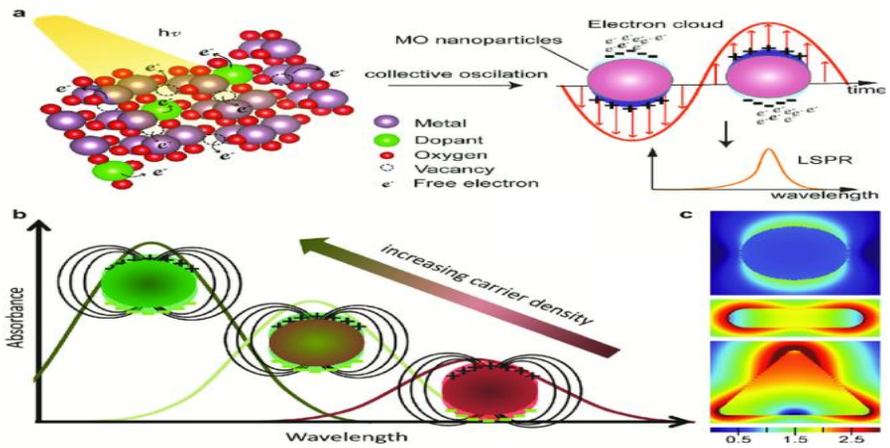
Different sized and shaped colloidal gold nanoparticles, such as nanorods, nanocages, and nanotubes, are excellent candidates for use as nanocarriers in drug delivery and biomedicine. They have emerged as significant candidates in the creation of cancer drugs and nanocarriers due to their stability, low cytotoxicity, strong attenuation coefficient of light from visible to NIR areas, and ease of manufacture. (Lee et al., 2021)

Au nanorods (NRs) were employed to treat cancer cells by laser-induced hyperthermia because of their NIR absorption properties. A variety of biomolecules, such as proteins, antibodies, and various biomarkers, can functionalize gold nanoparticles because of their special characteristics. They have

become superior photothermal agents in cancer treatment during the last 20 years due to their high molar absorption coefficient in the visible to near-IR region and surface plasmon resonance (SPR) (Wang et al., 2021).

Gold nanoparticles are also the perfect nanocarrier for reversibly binding both hydrophilic and hydrophobic drugs. The Khandelia group enclosed model hydrophilic and hydrophobic compounds, doxorubicin (Dox) and pyrene (Pyr), inside Au NP–Lysozyme agglomerated particles. The results imply that the newly created Au NP–Lysozyme agglomerate-based nanocarriers can serve as multimodal drug delivery vehicles and have great promise for drug loading and release procedures. (Romain et al., 2023)

However, it has been shown that Au NPs are efficient agents for photodynamic treatment. By covalently attaching the anti-HER2 monoclonal antibody to the PEGylated gold nanoparticles, a 4-component photodynamic agent (antibody-zinc phthalocyanine-PEGylated GNPs) was created and utilized as a possible medication for targeted photodynamic cancer therapy in breast cancer. Additionally, gold nanoparticles are presented as an. (Song et al., 2021).



(a) Schematic of localized surface plasmon resonance. Left: light irradiation of free electrons in MO nanoparticles. Right: resonance oscillation of electron cloud in MO nanoparticles. Adapted with permission. 2 Copyright r 2011, Nature Publishing Group. (b) Illustration of LSPR variation against the change of free charge carrier concentration in doped metal oxides. Reproduced with permission. 62 Copyright r 2017, Elsevier. (c) Simulated electric field intensity enhancement contour map of Au nanoparticles with the same volume and different shapes. . (Ding et al., 2021)

VI. Magnetic nanoparticles

Magnetic nanoparticles (MNPs), a particular kind of inorganic nanomaterials, are superparamagnetic and can be utilized as contrast agents in magnetic resonance imaging (MRI), site-specific medication and gene delivery, and diagnostic agents when an external magnetic field is present. (Wang et al., 2021)

They are typically coated with various water-soluble molecules, such as cationic polymers (like PLL, PEI), cationic lipids, and dendrimers (like polyamide amine, PAMAM), to create these biocompatible MNPs for biological applications. MNPs can be coupled with appropriate biomolecules, such as antibodies and positively charged amino acids, to enhance their absorption by tumors for target-specific delivery . (Umapathi et al., 2022)

Additionally, magnetic nanoparticles' cellular transport and selectivity can be enhanced. To improve MRI of prostate cancer, a biocompatible iron oxide MNP was coupled with the antibody J591, which targets the prostate-specific membrane antigen (PSMA). When compared to MNP alone (non-targeting MNPs), PSMA-targeted MNPs can dramatically improve the magnetic resonance contrast of prostate tumors. . (Zhao et al., 2024)

VII. Silver Nanoparticles

Because of silver's antibacterial properties, which have been studied by numerous civilizations for at least 6,000 years, silver nanoparticles (AgNPs) make up a sizable percentage of nanotechnology-based medical goods. Furthermore, AgNPs' electrical, thermal, and optical characteristics make them intriguing for use in medicine. (Bairagi et al., 2022)

The main issues with AgNPs' application in medicine at the moment center on reducing their unwanted biological consequences, such as cells producing more reactive oxygen species (ROS) and less ATP (Li et al., 2021)

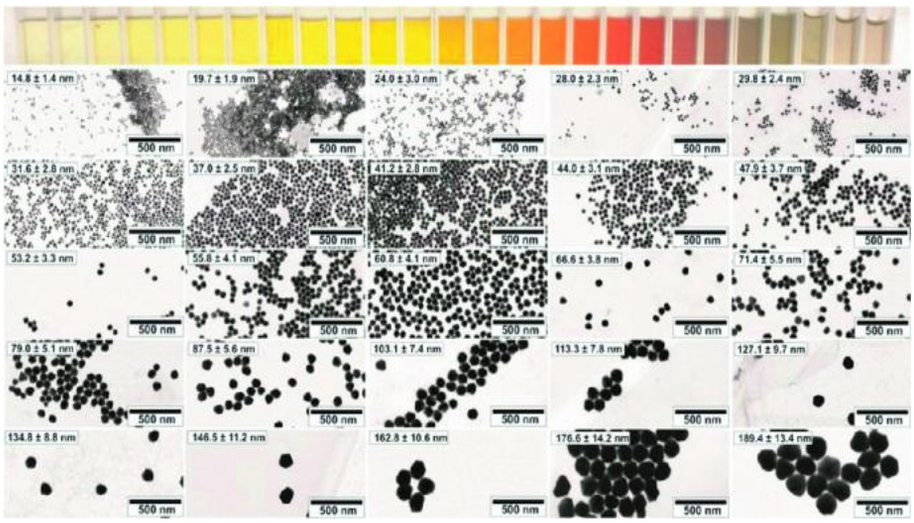
AgNPs are produced chemically, physically, or biologically. Chemical treatments are frequently used because they are inexpensive, simple, and operate well. Chemical syntheses were generally separated into two phases: growth and nucleation (Lin et al., 2020).

A silver compound and a reducing agent, such as sodium borohydride ($NaBH_4$) or silver nitrate ($AgNO_3$), react during nucleation (Servatan et al., 2024).

The growth phase follows, during which the size and shape of the particles are determined (Yang et al., 2020).

Following development, spherical AgNPs show a distinctive 420 nm plasmon resonance band. (Li et al., 2023).

However, depending on the AgNPs' size, shape, and chemical surface, this band may move from 350 to 700 nm. Figure 2 displays various AgNP colloidal dispersions with diameters ranging from 10 to 200 nm (Choi et al., 2021).



Electron microscopy of AgNPs with different sizes that were synthesized via reduction of silver nitrate in a method mediated by nucleation with kinetically controlled growth **(Khan et al., 2021)**

Although the physical techniques used to synthesize AgNPs are notable for their rapidity, they frequently result in NPs with a high polydispersity index. Furthermore, a lot of methods need a lot of energy to keep the pressure and temperature high. The physical approaches are distinguished by a top-down approach, in contrast to the chemical ones (Ai et al., 2021).

The biological approaches, which are based on the bioreduction of metal ions, rely on the activity of biomolecules that may reduce ions or ionic compounds, such as enzymes and polysaccharides. This reduction can be made by bacteria, yeasts,

fungi, and plants, which can then create nanoparticles of various sizes. One of the earliest species in which AgNP production was documented was the silver-resistant Pseudomonas stutzeri AG259 bacterium strain (Canaparo et al., 2020).

The right synthesis method, which permits regulating the release of silver ions or silver ionic complexes—to which antibacterial activity is frequently attributed—determines the antimicrobial qualities of AgNPs. Apart from the impact of silver ions, research also shows antibacterial activity as a result of the buildup of silver particles in the cell membrane, which compromises the membrane's integrity. (Bedair et al., 2021)

AgNPs' size is also thought to contribute to their antibacterial activity. According to certain research, the primary antibacterial mechanism for larger NPs is the release of silver ions, while the activity of silver nanoparticles smaller than 10 nm (diameter) originates from the nanoparticle itself (Tazwar et al., 2023).

This unclear effect based on AgNP size remains a challenge. Moreover, studies on the antibiotic activity of oxidized and zero valence AgNPs in *Escherichia coli* revealed that zero valence nanoparticles did not present harmful effects on bacteria (Mahmoudpour et al., 2021).

VIII. Magnetic Iron Oxide Nanoparticles

For many years, magnetic nanoparticles have been employed as ferrofluids, which are colloidal dispersions with reduced magnetic dipolar interactions that do not precipitate or aggregate when subjected to low magnetic or gravitational pressures due to their size and surface coatings. (Abd Elkodous et al., 2021)

Their capacity to react to an external magnetic stimulus is what makes them interesting and useful in the medical area. The nanoparticles show magnetization when a magnetic field is applied in the superparamagnetic zone. As a result, there are fewer side effects in living tissues since the interaction with external magnetic fields is limited to the magnetic NPs environment. Furthermore, when the external cues are eliminated, the magnetic field effect vanishes (Montiel Schneider et al., 2022).

Due to their water dispersity, which is necessary for in vivo applications, magnetic nanoparticles have a lot of promise for usage as theranostic agents in medical applications. (Chen et al., 2020)

Because of this, one crucial factor that should be taken into account while designing theranostic platforms is the biocompatible nature of magnetic nanoparticles. Because they can retain their magnetic characteristics at body temperatures, iron oxides like magnetite (Fe3O4) and maghemite (γ-Fe2O3) are the most popular magnetic nanoparticles for medical purposes. (Wang et al., 2021)

With a high spatial resolution (c.a. 50 μm), gadolinium- and manganese-based NPs, as well as superparamagnetic iron oxide nanoparticles (SPIONs), have been investigated as contrast agents in magnetic resonance imaging, enabling in vivo cell and organ imaging.. (Ramburrun et al., 2022)

Given that they may be produced in a range of sizes and configurations, superparamagnetic iron oxide nanoparticles, or SPIONs, are particularly interesting for use in medical applications. (Chua et al., 2023)

In order to enhance the magnetic characteristics of Fe3O4 and γ-Fe2O3, scientists have created ferrite structures, which assume an MFe2O3 molecular structure by substituting additional bivalent transition metals (M) for the Fe^{2+} ions. The ferrites based on nickel, cobalt, manganese, and zinc are the most researched for biological applications. For instance, cobalt was utilized in the creation of a carbon-coated FeCo-based theranostic agent. (Shepherd et al., 2021)

The combined effects of magnetothermal and photothermal heatings led to improved in vivo imaging, which was evaluated using either magnetic resonance imaging or photoacoustic methods. Additionally, the nanoparticles demonstrated therapeutic qualities since the localized temperature increase decreased. (Li et al., 2021)

The most popular chemical technique for creating SPIONs is coprecipitation, which essentially consists of two steps: the nucleation and development of the NPs. Typically, a bivalent transition metal ion and a saline solution containing Fe3+ are combined in stoichiometric amounts and heated in an inert atmosphere. (Amiri et al., 2020)

After adding a strong base to the solution, the salts begin to hydrolyze alkalinely, forming nanoparticles. A number of variables, including the solution's pH and temperature, are crucial for regulating the magnetic nanoparticles' shape and size distribution. The size distribution of the nanoparticles can also be controlled using polymers or surfactants. The coprecipitation method's ease of use, inexpensive ingredients, and ability to produce nanoparticles in watery. (Bao et al., 2021)

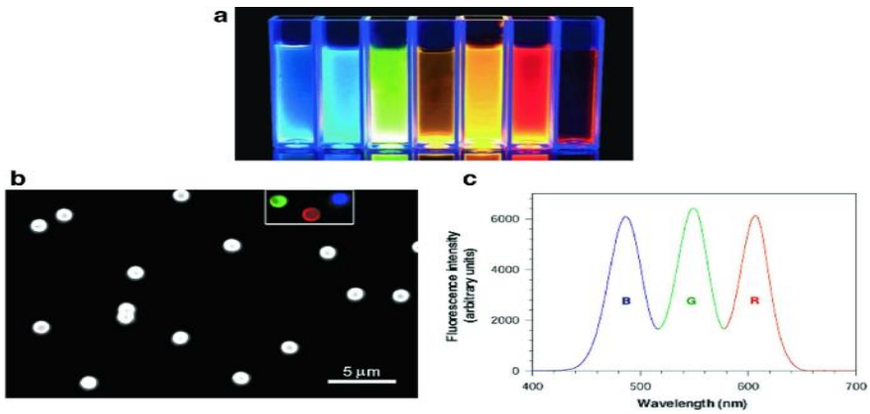
An illustration of using heat to treat cancer magnetically in naked mice (tumor cell U87MG). The animals were exposed to an alternating magnetic field while the magnetic nanoparticles (CoFe2O4@MnFe2O4), doxorubicin, and Feridex® IV (Berlex Laboratories) were administered directly into the tumor.. **(Sun et al., 2021)**

IX. Quantum Dots

With typical sizes ranging from 2 to 10 nm, inorganic quantum dots (QDs) are semiconductor colloidal particles with special photophysical characteristics. These nanomaterials have been regarded as a potent tool for biomedical applications involving luminescence, particularly as fluorescent probes, while having a significant variety of uses in photonics and electronics. (An et al., 2021)

QDs offer notable advantages over traditional organic fluorescent probes because of their high optical characteristics, which include a high extinction coefficient, a quantum yield, and photostability with minimal photobleaching. Furthermore, as Fig. 4 illustrates, QDs' broad and narrow emission bands enable a symmetric luminescence spectrum from the ultraviolet (UV) to the near-infrared (IR) region, enhancing their biomedical use.. (Zhang et al., 2020)

Since QDs have a longer emission lifespan than organic fluorophores and an active surface that can combine their fluorescent features with the attached biomolecule's (bio)chemical functionalities, they have in fact demonstrated significant promise for in vitro investigation.. (Liu et al., 2021)



For CdS quantum dots stimulated at 370 nm, distinct emission colors are found between 477 and 696 nm. b Fluorescence picture of colorful spheres with QDs attached and fluorescence intensities carefully adjusted. c The QD-marked spheres' fluorescence spectra displays three distinct peaks with near-intensities at 484, 547, and 608 nm.. (Soares et al., 2020)

Chemical elements from groups II–VI and III–V, such as CdSe, CdTe, ZnSe, InP, and InAs, are typically used to create QDs. The most popular method for producing QDs is organic synthesis, which involves quickly injecting an organometallic precursor into an organic solvent for high-temperature nucleation and subsequent growth at lower temperatures. Because of their potential toxicity, QDs cannot be directly used in biological applications due to their chemical production, even though their size can be controlled to a high degree. (Sharma et al., 2023)

A wet chemical method was employed to create water-stable CdS modified with 2-mercaptoethanol, and some optimizations were reported that used an aqueous media to circumvent the organic phase. (Ramburrun et al., 2022)

High molecular mass organic compounds, such as 3-glycidyloxypropyl) trimethoxysilane or 5-norbornene-2-nonanoic acid, were employed to enhance stability in order to get around these problems. The increased fluorescence quantum yield of core-shell QDs is an outstanding feature. (Mahmoudpour et al., 2021)

While the outermost layer, or shell, is utilized to passivate the QD's surface and lessen chemical deterioration from environmental changes like pH or the presence

of reactive species, the interior core is in charge of optical qualities like absorption and emission. To ensure the physical separation of the optically active core from the surrounding medium, a second semiconductor material often forms the shell. (Soares et al., 2020)

X. Ceramic Nanoparticles

Drugs, proteins, DNA, and RNA can be loaded into ceramic nanoparticles, which are porous inorganic systems with adjustable pore diameters. Common examples of ceramic nanoparticles are silica, titanium oxide, calcium phosphate, and alumina nanoparticles. Because of their remarkable stability, changes in temperature or pH alone cannot alter their size or porosity (Ramburrun et al., 2022).

Concerns remain regarding ceramic INPs' protracted breakdown periods, toxicity, and organ accumulation despite their inert nature.A common synthetic method for creating silica nanoparticles is the Stöber procedure, which involves hydrolyzing an ethanol/ammonium solution and then condensing it with tetraethoxisilane (TEOS) at 70 °C.. (Shepherd et al., 2021)

This technique uses a variety of proteins and polymers to modify particle surface chemistry to give the required QDs features, such as a positively charged surface or biocompatibility. A cotton textile and silica nanoparticle-based drug delivery system that contained anti-inflammatory compounds such salicylic acid, ibuprofen, and diclofenac demonstrated good release qualities in vivo, creating new opportunities to enhance the topical cutaneous applications of silica nanoparticles. (Mahmoudpour et al., 2021)

A variety of synthetic methods, including precipitation from supersaturated solutions containing calcium and phosphate ions, can be used to produce calcium phosphate INPs. The later synthesis techniques, however, provide nanoparticles with diverse size distributions in spite of their low cost. The sol-gel technique, which creates a colloidal suspension (sol) by hydrolyzing metallic organic precursors, can yield homogeneous nanoparticles.. (Akgöl et al., 2021))

By dissolving $CaHPO_4 \cdot 2H_2O$ in aqueous solution under alkaline conditions, then adding acetyltrimethylammonium bromide, the hydrothermal process can be

performed for two hours at 150 °C. The potential for dual surface functionalization, which enables the inclusion of various molecules both inside and outside the pores and co-delivery to the targeted tissues, is an intriguing characteristic offered by ceramic nanoparticles. (Ramburrun et al., 2022)

The co-administration of two well-known chemotherapeutics, doxorubicin and cisplatin, using a matrix scaffold and calcium phosphate beads to treat osteosarcoma. In order to produce silica nanoparticles that are non-cytotoxic and free of corona, dual functionalization is also being investigated.Additionally, ceramic nanoparticles (NPs), particularly ZnO and TiO2, are utilized to enhance sunscreens' protective qualities.. (Soares et al., 2020)

XI. Inorganic Nanoparticles-Based Systems in Biomedical Applications of Stem Cells: Opportunities and Challenges

It is well known that stem cells are capable of pluripotent differentiation and infinite self-renewal. They can develop into multipurpose cells in some circumstances. Stem cells can be classified as either adult stem cells (somatic stem cells) or embryonic stem cells (ES cells) based on their developmental stage. (Shepherd et al., 2021)

Three types of stem cells can be distinguished based on their capacity for development: totipotent stem cells (TSC), pluripotent stem cells, and unipotent stem cells. Mesenchymal stem cells (MSCs) and other stem cells are currently being employed extensively in clinical trials.. (Akgöl et al., 2021))

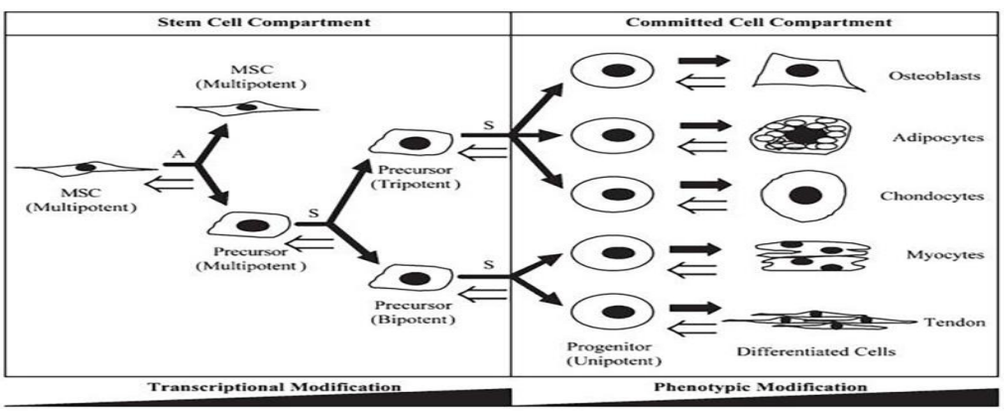
Because so many MSCs are found in tissues, MSCS is ideally suited for future use in clinical, regenerative medicine, and experimental settings. MSCs can be isolated from a wide range of tissues, including adipose tissue, bone marrow, menstrual blood, endometrial polyps, and umbilical cord. MSCs can be made to develop into a wide range of tissue cells, including nerve, heart, liver, bone, cartilage, tendon, fat, epithelium, and more, under particular in vivo and in vitro conditions. (Mahmoudpour et al., 2021)

Since Ernest A. McCulloch and James E. Till discovered hematopoietic stem cells in mouse bone marrow cells, stem cells—more especially, MSCs—have demonstrated significant therapeutic potential through the process of cell

differentiation that creates a specific tissue to cure a variety of illnesses (Ramburrun et al., 2022)

The stem cells that are transplanted into the body replace or repair damaged cells or tissues in order to treat the disease by differentiating into comparable cells and tissues. Therefore, there is a lot of promise for using stem cells in clinical settings to treat a variety of illnesses. (Shepherd et al., 2021)

One of the main obstacles in stem cell therapy is directing the differentiation of stem cells in vivo while concurrently monitoring transplanted stem cells or detecting the differentiation of stem cells, despite the fact that stem cells have enormous potential as a revolutionary treatment for major human diseases.. (Solangi et al., 2024)



The differentiation direction of stem cells. **(Solangi et al., 2024)**

Because of their unique optical, electrical, magnetic, catalytic, and biocompatible qualities, as well as their controllable size, inorganic nanoparticles—which, in general, include a variety of metals, semiconductor materials, and metal oxide nanoparticles—have been extensively researched as therapeutic drugs for the treatment of disease in the biomedical field. (Mahmoudpour et al., 2021)

Because of these characteristics, inorganic nanoparticles are anticipated to have potential uses in enhancing human health and well-being, including early disease detection, diagnosis, treatment, and follow-up.. (Akgöl et al., 2021))

The potential of inorganic nanoparticles for the creation of efficient and multipurpose cancer therapies is demonstrated by the numerous cancer treatment

systems based on these particles that have been developed over the past 20 years, such as drug delivery, photodynamic therapy, nanoprobes, and hyperthermia. (Soares et al., 2020)

In general, systems based on inorganic nanoparticles comprise lanthanide-based, semiconductor-based, iron-based, silicon-based, carbon-based, gold-based, and several other types of inorganic nanoparticles.. (Ramburrun et al., 2022)

More and more inorganic nanoparticles are being used in the field of stem cell biomedical application due to the benefits and effective usage of inorganic nanoparticle-based systems in cancer therapy in recent years. Inorganic nanoparticles have the following benefits: they can be used to create a stable physical and chemical environment, simulate a nanoenvironment that influences stem cell behavior and function, achieve long-term regulation, and track the fate of stem cells in vivo. (Shepherd et al., 2021)

Second, different inorganic nanomaterials have distinct morphologies and structures. A platform for spatially regulated stem cell differentiation and other methods for directional regulation of stem cell destiny are made possible by the interaction of nanomaterials with cells.. (Solangi et al., 2024)

Thirdly, inorganic nanomaterials can have varying functions and behaviors on stem cells in different situations because they typically have an effect on the stem cells that come into touch with them through endocytosis or exocytosis, but they have minimal effect on other cells. Numerous inorganic nanoparticle types, including upconverting nanoparticles (UCNPs), quantum dots (QDs), magnetic nanoparticles (MNPs), mesoporous silica nanoparticles (MSNs), graphene oxide (GO), gold nanoparticles (AuNPs), and carbon nanotubes (CNBS), have been employed thus far in stem cell research and applications. (Akgöl et al., 2021))

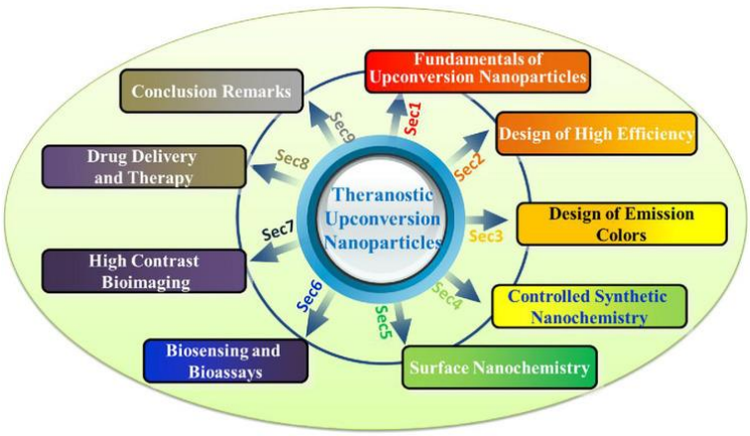
In order to better understand human diseases and create strategies for their prevention and treatment, multifunctional inorganic nanoparticle-based systems have been developed and show significant promise in the field of stem cell biomedical applications.. (Mahmoudpour et al., 2021)

A summary of the various types of inorganic nanoparticles, including UCNPs, QDs, MNPs, MSNs, GO, AuNPs, and CNBS, that are currently being developed

in stem cell therapy is provided. The selection of promising inorganic nanoparticles was used for stem cell study, including real-time stem cell monitoring, stem cell differentiation detection, and control of cell behavior of adhesion, spreading, and multi-differentiation by inorganic nanoparticles modified substrate. (Ramburrun et al., 2022)

XII. Upconversion Nanoparticles (UCNPs)

Upconversion nanoparticles (UCNPs), which are typically made of trivalent lanthanide ions, have the ability to absorb NIR light and convert it into UV or visible light. Thus, in biomedical applications, NIR-to-UV/visible UCNPs have garnered a lot of interest.. (Shepherd et al., 2021)



All kinds of different biomedical application of UCNPs. (Soares et al., 2020)

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