Review Article

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ROLE OF INORGANIC PARTICLES FOR THE FORMULATION OF NANOPARTICLES: A REVIEW

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ABSTRACT

Inorganic particles do not have carbon in their backbone and are produced through various geochemical processes, i.e. they are not biological in nature. It is a common practice to use inorganic particles to formulate nanoparticles as their size is near nanoscale dimensions. Various inorganic particles such as silver, gold, silica, alumina and magnetite have been used to fabricate nanoparticles. These nanoparticles are used in different fields, such as magnetic recording, chemical sensing, anti-microbial assays and enzyme immobilization. They have several advantages due to their increased surface area-to-volume ratio, enhancing their reactivity. This review will discuss various inorganic particles used for nanoparticle preparation and their structure, properties, and applications in biomedical engineering. The major applications of formulated nanoparticles are used in biomedicines for drug delivery. They can deliver the drug to the specific site by crossing many biophysical, biochemical and biological barriers.

Keywords: Inorganic particles, nanoparticles, specificity, drug delivery.

INTRODUCTION

Nanotechnology plays an important role in the field of science and engineering and has advanced the work to the molecular and cellular levels. The unique properties of nanomaterials make them an excellent tool of the future; however, their real applications in life sciences are limited in the present time[1-2]. Inorganic particles are an efficient tool for fabricating nanoparticles[3] and immobilization matrices for biomolecules like antibodies, peptides, proteins, ligands, and oligonucleotides[4]. The nanoparticles are smaller and thus provide a larger surface area to volume ratio; hence, the detection devices built using them are portable and have low operating costs. One of the remarkable properties of metallic nanoparticles is their superplastic behaviour. These nanoparticles offer many advantages, such as a low amount of sample and fast and sensitive detection[5]. Efficient detection is possible as the energy band gap is increased when the particle dimensions of semiconductor materials are reduced to a size smaller than or equal to Bohr's radius. When the size of noble metals is reduced below the electron mean free path, the absorption in the visible-near-UV region increases significantly[6].

INORGANIC NANOPARTICLES

Magnetic Nanoparticles

Magnetic nanoparticles have a surface effect and finite sizes that dominate their individual magnetic properties, and due to this, they offer certain advantages such as a high saturation field, shifted loops after cooling, and superparamagnetism[7]. The ferromagnetic particles, below the size of less than 15 nm, contain a single magnetic domain, which gives them uniform magnetization in any field. The behaviour of magnetic particles and atomic paramagnets above blocking temperature is similar. The magnetic nanoparticles are used widely such as in magnetic recording media, magnetic inks for bank cheques, magnetic resonance contrast media, magnetic seals in motors, and therapeutic agents in cancer treatment.

Synthesis
Magnetic nanoparticles can be synthesized using techniques such as gas phase deposition, water in oil microemulsion and sol-gel hydrothermal method.

Gas Phase Deposition Method: In this method, iron organic salts or organometallic compounds are decomposed at high temperatures so that iron particles are precipitated from the gas phase. This process of thermal decomposition is known as pyrolysis.

Water In Oil (w/o) Microemulsion Method: Nanosized water droplets are stabilized using surfactant molecules at water/oil interphase after being dispersed into the oil. Different types of nanoparticles, like silica-coated iron oxide nanoparticles, magnetic polymeric iron oxide nanoparticles, and iron oxide nanoparticles, have been prepared using this method.

Applications
Magnetic nanoparticles play a significant role in bio-nanotechnology and biological sample preparation. Magnetic nanoparticles enhance the capturing of targeted bacteria, and this process is known as immune-magnetic separation. The nanoparticles are modified with carboxylic acid, thiols, or amines[8], then specific antibodies are chemically grafted on them, and under controlled conditions, the bacteria are easily recognized and extracted using a magnetic field. Using immune-magnetic separation, *Salmonella* bacteria were isolated from milk samples[9].

Silica Nanoparticles

Silica nanoparticles are considered an important candidate for diagnosing several diseases, drug delivery systems, gene therapy, and bioimaging[10]. Silica nanoparticles (SNPs) are prepared on a large scale as these are biocompatible and highly hydrophobic, with a large surface area and pore volume.

Synthesis

The SiNPs with narrow size distribution and controlled size are achieved using a sol-gel process first used by those who synthesized SiNPs of size 0.05 to 2 nm with the help of ammonium solution catalyst and TEOS (tetraethyl orthosilicate)[11]. The size and morphology of SiNPs are affected by sodium silicate concentration, reaction temperature, and amount of alcohol present in the reaction mixture[12].

Applications

Silica nanoparticles are used for different applications, such as supporting fluorescent labels used in bioimaging. Nucleic acids and proteins can be detected using multi-coloured FRET (fluorescence resonance energy transfer) nanoparticles synthesized using three organic dyes, and these nanoparticles can be excited using a single wavelength to generate multiple emission signatures[13]. SiNPs can also be used in cancer detection by labelling the SiNPs (30 nm) using fluorescein isothiocyanate (FITC)[14]; human lung adenocarcinoma was detected using FITC-SiNPs conjugated with cell-penetrating peptide, TAT (trans-activating transcriptional activator)[15]. These nanoparticles (mesoporous SiNPs) could also be used in drug delivery due to their surface construction, which makes them an efficient carrier of different drugs and molecules[16].

Quantum Dot Nanoparticles

The semiconductor nanocrystals whose electronic band structure changes with three-dimensional particle size confined within a few nanometres of space are called quantum dots (QDs). They possess photostability, noble optical properties, and well-defined spectral properties, so they are used as biomolecular labels, detection probes,[17,] and *in vitro* biomedical imaging.

Synthesis

QDs can be synthesized using different materials, such as a mixture of type III-V compounds (GaAs, InAs, GaP, GaN, etc.), type II-VI compounds (ZnS, CdS, ZnO, CdSe, ZnSe, etc.) or pure materials like selenium[18]. The most common types of QDs are generated by a mixture of cadmium and selenium (CdSe). Their fluorescence varies from blue to red depending on the size of the QD formed, ranging from 2-10 nm[19]. The main part of the QD structure is its core shell, which contains nearly 1000 atoms[7] and is coated by a zinc sulphide (ZnS) layer to protect it from chemical degradation[20].

Applications

Fluorescent molecules such as rhodamine and fluorescein are used to label biomolecules such as antibodies to enhance diagnostic sensitivity[21]. Inorganic semiconductor QDs are used for biomedical diagnosis due to their non-fluorescent bleaching. Compared to organic fluorescent molecules, QDs have narrow and sharp emission peaks and broader excitation spectra, which allow them to be excited by single light sources and do not have signal overlap. These are also used for capturing images and detecting targets in real-time and in multiple labelling experiments like bar code[22].

SHG-active Nanoparticles

The Second Harmonic Generation (SHG) nanoparticles are the recent type of nanoparticles used in bioimaging. They possess unique optical properties, such as they lack a centre of inversion in their crystalline structure and without phase-matching conditions, they can generate second harmonic signals[23]. In the Two-Photon Excited Fluorescence (TPEF), one photon (2ω frequency) is converted from two incident photons (ω frequency), and this frequency conversion efficiency is due to the volume effect and is very high[24]. This high-frequency conversion efficiency is helpful in the detection of nanoparticles approximately 100 nm in size. On the other hand, in SHG, the virtual states are involved, and the initial energy is not lost during internal conversion or non-radiative vibrational relaxation. Due to this property, SHG-active nanoparticles are used in detecting photostability, multiphoton microscopy,[25] and deep imaging[26] of tissues and living cells [27,28] as good resolution is provided by the presence of two photons at the microscope's objective. This imaging could be enhanced by coupling the nanoprobes with quantum dots and fluorescent dyes.

Synthesis

SHG-active nanoparticles can be synthesized through different physical and chemical routes. By varying the concentration of reactants, $LiNbO_3$ nanoparticles of controlled size (<50 nm) can be synthesized[29]. These nanoparticles could also be obtained by reduction of Nb salts followed by hydrolysis by LiH. SHG-active nanoparticles made up of ZnO and $BaTiO_3$ are commercially available[30,24] and are prepared by hydrothermal treatment and sol-gel processes [31,32].

Applications

SHG-active nanoparticles can be used to detect cells (Keratin-forming tumour cell line HeLa) using high contrast ZnO nanoparticles incorporated with folic acid and stabilized by phospholipid micelles[33]. $BaTiO_3$ (barium titanate) nanocrystals modified by silane-conjugation with aminopropyltriethoxysilane (APTES) followed by amine group modification and IgG antibody functionalization can be used for *in vitro* cell imaging[30]. $KNbO_3$ nanoparticles can be used to obtain real-time images of cardiomyocytes derived from embryonic stem cells during embryonic stem cell evolution[34]. The novel and highly stable L-asparaginase (L-ASP) entrapped gelatin alginate nanoparticles (GANp) have been synthesized to develop an easily reproducible, sensitive, and selective fibre optic asparagine biosensor[35].

CONCLUSION

It has been found that with technological advancements, the focus is shifting towards nanotechnology. Several materials have been used to develop nanomaterials; inorganic particles are one of the efficient tools for the fabrication of nanoparticles. Gold, silver, iron, and silica are used for nanoparticle synthesis. Recently, SHG-active nanoparticles have been synthesized, which have proved to be an efficient tool for diagnosing different diseases and bioimaging. Inorganic nanoparticles have revolutionized the medical and biological areas and paved new paths toward improving human health.

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