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Review on mesoporous silica nanoparticles.

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Abstract

This study presents a concise examination of the synthesis of various mesoporous silica nanoparticles (MSNs) and their applications as nanocarriers for drug delivery. MSNs possess a small pore size, which contributes to their large surface area and porosity. These characteristics can be easily adjusted, giving MSNs an advantage over other nanoparticles in the field of medicine and pharmacy. The study explores both past and current trends in MSN technology, as well as the potential for drug loading, methods to increase loading capacity, functionalization, and release of bioactive substances. It has been discovered that the synthesis method employed for certain types of MSNs leads to improved drug loading. The functionalization of nanoparticles not only facilitates the successful loading of bioactive substances into their pores, but also effectively controls drug release. Additionally, these versatile nanoparticles enhance the solubility of poorly-soluble drugs, addressing a significant challenge in drug absorption.

Keywords: - mesoporous silica nanoparticles, synthesis, morphological characteristics, soft templating, Hard templating.

Introduction

In recent times, porous silica has emerged as a highly significant advancement in the field of nanotechnology. These materials possess exceptional characteristics such as thermal stability, chemical inertness, affordability, ease of synthesis, non-toxicity, biocompatibility, and excellent adaptability for surface functionalization. As a result, experts worldwide have devoted considerable attention to utilizing porous silica in various domains, including catalysis, sensing, energy applications, optically active materials, drug delivery, and more.[1] In the present era, modern nanotechnology has emerged as a fundamental element of scientific advancements. Throughout the years, the diagnosis and treatment of diseases have consistently achieved significant progress, largely attributed to the implementation of nanotechnology in the realm of biomedicine.[2]

Nanoparticles: -

Nanoparticles can be defined as entities with dimensions ranging from 1-100 nm, which, owing to their size, exhibit distinct properties compared to the corresponding bulk material. Currently, various metallic nanomaterials are being manufactured utilizing copper, zinc, titanium, magnesium, gold, alginate, and silver. Nanoparticles consist of a minimum of one hundred atoms and are commonly referred to as nanospheres or nano capsules. They serve as matrix systems in which drugs are uniformly dispersed. Nano capsules, on the other hand, involve the encapsulation of drugs within a polymeric membrane.[3]

- **Types of nanoparticles:**[28]

1) Organic nanoparticles.
2) Inorganic nanoparticles.

1) **Organic nanoparticles.**

1. Polymeric nanosphere.
2. Polymeric nano capsule.
3. Polymeric micelle.
4. Liposome.
5. Dendrimer.

2) **inorganic nanoparticles.**

1. Mesoporous silica nanoparticle.
2. Carbon nanotube.
3. Iron oxide nanoparticle.
4. Gold nanoparticles.
5. Quantum dot.

- **Advantages of nanoparticles**: -

1. Enhanced bioavailability due to increased solubility.
2. Targeted delivery of drugs.
3. Prolonged drug resistance.
4. Biodegradable polymers used in nanoparticle preparation, reducing toxicity.
5. Administration through various routes, including oral, parenteral, and intra-ocular.
6. Easy incorporation of drugs without the need for chemical reactions.
7. Matrix constituents can alter degradation characteristics and controlled release patterns.[3]

- **Disadvantages of nanoparticles**:

1. Ostwald ripening, leading to the formation of aggregates/agglomerates due to high free energy of nanoparticles.
2. More complex operational procedures.
3. Higher chances of contamination.
4. Difficult handling of nanoparticles in liquid and dry forms due to their small size and large surface area.
5. Increased reactivity of nanoparticles towards the external phase due to their small size and large surface area.[4]

- **The utilization of nanoparticles encompasses a wide range of applications in various fields. These applications include, but are not limited to:**

1. Drug and gene delivery: Nanoparticles have shown great potential in delivering drugs and genes to specific target sites within the body, allowing for enhanced therapeutic efficacy and reduced side effect.
2. Tissue engineering: Nanoparticles can be employed in the field of tissue engineering to promote cell growth and regeneration, aiding in the development of functional tissues and organs.
3. Protein detection: Nanoparticles can be utilized as sensitive probes for the detection and quantification of proteins, enabling researchers to study protein interactions and monitor disease biomarkers.
4. Bio-detection of pathogens: Nanoparticles can be engineered to detect and identify various pathogens, facilitating rapid and accurate diagnosis of infectious diseases.
5. DNA probing: Nanoparticles can be employed as probes to study and manipulate DNA, enabling researchers to gain insights into genetic information and develop advanced diagnostic tools.
6. Destruction of tumour cells through heating: Nanoparticles can be selectively targeted to tumour cells and then activated by external stimuli, such as heat, to induce localized hyperthermia and destroy cancer cells.

These applications highlight the immense potential of nanoparticles in advancing various fields, offering promising avenues for further research and development.[3]

Mesoporous silica nanoparticles: -

Mesoporous silica nanoparticles (MSNs), which are silica nanoparticles with mesopores, have become increasingly popular in recent years. Their uniform and adjustable pore size, ability to be easily functionalized, and internal and external pores, as well as their gating mechanism for pore opening, make them a unique and promising drug carrier. Researchers have successfully utilized these carriers to load a variety of cargo, including drugs, proteins, DNA, and RNA [5,6]

Types of mesoporous silica nanoparticles: -

Various surfactants have been utilized to create MSNs with distinct structures. The synthesis process involves diverse designs and controls, leading to variations in the morphologies, pore sizes, and structures of the MSNs.[7]

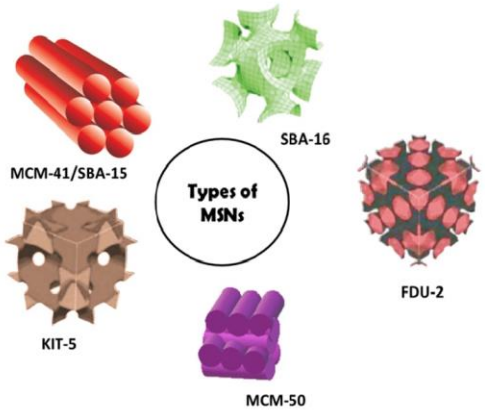

Figure.1 Types of mesoporous silica nanoparticles.

Advantages:

- The adjustability of size and shape.
- Precisely defined surface characteristics.
- Elevated pore volume and surface area.
- Significant loading capacity.
- Substantial bioavailability

Disadvantages

- Challenging in the preparation of a well-organized structure.
- Varied size distribution.
- Creation of a stable colloidal suspension.[8]

Morphology of Mesoporous Silica Nanoparticles:[26]

1) Particle size:

Mesoporous silica nanoparticles can be produced through the use of surfactants in an aqueous solution, which can be either charged or neutral. The polymerization of silicates (an ester of ortho silicic acid) is facilitated by the surfactant. The factors that influence the size and shape of mesoporous silica nanoparticles include: -

- The rate of hydrolysis.
- The level of interaction between the assembled template and silica polymer.
- The condensation of the silica source.

By controlling the pH, using different templates, and employing co-solvents, we can manipulate these variables. Stucky et al. successfully synthesized hard mesoporous silica spheres with sizes ranging from hundreds of microns to millimeters at the oil-water interphase. They achieved this by using a high concentration of template and hydrophobic auxiliary. The stirring rate also plays a crucial role in determining the particle size of MSNs. Slow stirring leads to the production of long fibers, while fast stirring results in the formation of fine powder. The effect of pH on the morphology of MSNs was investigated by Ozin et al., who found that under mildly acidic conditions, spherical mesoporous particles ranging from 1-10 μm are formed. Brinker et al. utilized a technique involving the evaporation of solvent from an aerosol containing the silica source and surfactant to synthesize MSNs ranging from 100-500 nm.

2)Pore size:

The parameters utilized to regulate the pore structure of MSNs include the amount of silica source and surfactant . The aggregation of surfactant in the solution is dependent on the pH and concentration of the solution. MSNs are synthesized at both acidic and basic pH levels, resulting in different pore structures. For instance, lamellar meso phases are formed at high pH (>12), while hexagonal structures are produced at basic pH (10-12) . Lin et al. achieved varying antibacterial effects in ionic liquid containing MSNs by altering the pore structure, transitioning from cylindrical channels to twisted ones . Hydrothermal treatment, either during synthesis or post-synthesis, is employed to adjust the pore width. The choice of surfactant with different hydrophobic chain lengths or the use of mesitylene as a swelling agent plays a crucial role in achieving the desired pore size . Pore expansion can be achieved by incorporating additives during synthesis, but additional tuning is necessary as additives can alter the hydrophobic-hydrophilic balance. Mesitylene is utilized as a pore

expander for MSNs, enlarging the pores from 3-5 nm without affecting the particle size. These MSNs with enlarged pores are then utilized as vehicles for delivering membrane impermeable proteins to cancer cells. In hydrothermal treatment during post-synthesis, a freshly prepared material is subjected to autogenic pressure at temperatures ranging from 373 K to 423 K, with or without additives, to increase the pore size without altering the morphology of pre-formed particles. Ying, Botella, and Corma demonstrated the control of pore size and particle size by utilizing a fluorocarbon-based surfactant in combination with a polymer-based surfactant. X-ray diffraction and transmission electron microscopy (TEM) are employed to measure the pore structure of MSNs, while nitrogen sorption is utilized to measure the pore width. The common mesophases in silicas with pore sizes are the 2D hexagonal p6m (MCM-41), the 3D cubic Ia3d (MCM-48), and the lamellar p2 (MCM-50).

3)Surface area:

The quantity of adsorbed pharmaceutical products is primarily determined by the surface area of the MSNs. To regulate the amount of drug incorporated in the matrix, two approaches are utilized: increasing or decreasing the surface area and modifying the surface drug affinity. This highlights the direct proportionality between surface area and the amount of drug adsorbed. MCM-41, with a surface area (SBET value) of 1157 m2g-1, can load 139 mg g-1 of alendronate under the same conditions, while SBA-15, with a surface area value of 719 m2g-1, can only load 83 mg g-1. This indicates that the surface area value is closely related to the maximum loading of the drug . In a separate study by Lin et al., the biocompatibility of MSNs with RBCs was investigated, and it was concluded that the large surface area of MSNs is rich in haemolytic silanol groups, which can cause high toxicity.

4)Pore volume:

Typically, the pore volume falls within the range of 2 cm3g-1 when the pore size is smaller than 15 nm, and the surface area is approximately 1000 m2g-1. The interaction between a drug and mesopores is a surface phenomenon, while inadequate drug-drug interactions can result in incomplete pore filling. The quantity of drug adsorbed can be determined by the pore volume. In the case of ordered mesoporous materials, repeated loading of the drug leads to significant filling of the mesopores, thereby increasing drug-intermolecular interactions within the wider pore space. This suggests that pore volume and the amount of drug loaded are directly proportional to each other.

Composition/ materials:

Tetraethyl orthosilicate (TEOS) SiC8H20O4, possessing a molecular weight of 208.33 g/mol, is utilized in conjunction with the surfactant Cetyltrimethylammonium ammonium bromide (CTAB) C19H42Br. Loss drying of 2% at 100°C is observed, resulting in a liquid crystal templating effect. Ethyl alcohol absolute ((CH3)2CO) with a molecular weight of 46.07 g/mol and poly (vinyl alcohol) (PVA) (C2H4O) n with a viscosity range of 25–32, degree of polymerization of 1700–1800, and pH range of 5–7 is also employed. Additionally, isopropanol CH3CH(OH)CH3, with a molecular weight of 60.10 g/mol, is utilized. [29]

Synthesis of mesoporous silica nanoparticles: -

Stober is credited as the originator of the technique for producing silica particles that are uniform in size and have spherical shapes. This method involves the hydrolysis of tetra alkyl silicates in a hydroethanolic solution, with ammonia acting as a catalyst. Over time, numerous adjustments have been made to this approach. One of the earliest modifications was introduced by Grun et al, who incorporated cationic surfactants such as n-hexadecyltrimethylammonium bromide and n-hexadecyl pyridinium chloride into the reaction mixture as templates. This modification resulted in the formation of the MCM-41 structure.

. The MCM-41 is a well-researched type of MSNs that possess a uniform and ordered arrangement of two-dimensional hexagonal mesopores. To prepare them, a combination of cetyltrimethylammonium bromide (CTAB), tetraethyl orthosilicate (TEOS), and a catalyst is used, along with sodium metasilicate (Na2SiO3) as the silica precursor. Kresge's team, on the other hand, used a solution containing hexadecyltrimethylammonium ion C16H33(CH3)3N+OH/Cl mixed with catalpa alumina tetramethylammonium silicate solution, and precipitated silica at 1:1 molar ratio of tetramethylammonium: SiO2. The combination was then heated at a temperature of 150ºC for 48h under pressure in a sterilizer. After cooling to room temperature, filtering, washing with water and air-drying, the solid product was calcinated at 540 ºC for 1h, first in flowing nitrogen, and thereafter in flowing air. It was discovered that substituting dodecyl trimethylammonium with hexadecyltrimethylammonium ion resulted in changes in the pore diameter of MCM-41. It was also concluded that varying the length of the alkyl chain of cationic type surfactants allows for nanoparticles with different pore sizes. Another method of increasing the pore diameter is by adding 1, 3, 5-trimethylbenzene. It was suggested that organic molecules should be solubilized in the hydrophobic inner part of micelles, causing an increased micellar size . It is known that CTAB self-aggregates into micelles when its concentration reaches the critical level for micelle formation (Figure 2). The silica precursors superpose at the surface of surfactant around the micellar polar head and form a wall around them. Removal of the surfactant results in the formation of MCM-41.

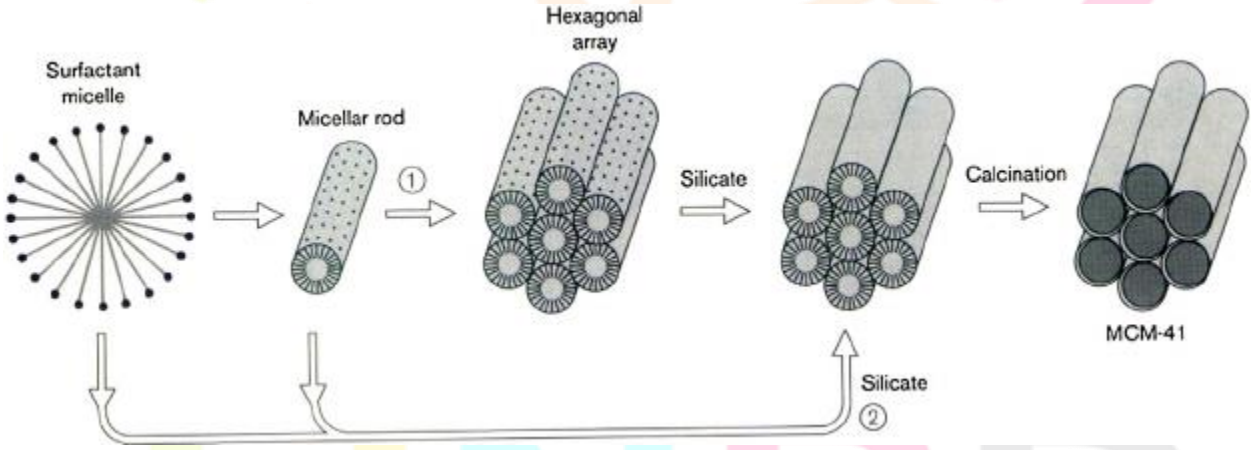

Figure.2. Scheme for synthesis of MCM-41 with a template of CTAB micelles.

By adjusting the molar ratio of the surfactant to silica, it is possible to control the size and shape of MCM-41, as well as the co-condensation of tetraethoxysilane and hydrophobic organ alkoxysilane. There are various methods available for precise control of the inner structure, pore size, and geometry, such as the use of organic swelling agents or cosolvents, pH control, temperature regulation, drying and stirring rates. When Na2SiO3 is used as a precursor, larger pores and higher specific surface areas are obtained due to an increase in the number of surfactant micelles. On the other hand, the use of TEOS leads to smaller pore sizes and lower surface areas. By adjusting the concentration and molar ratio of CTAB and NaOH, MCM-41 can be generated with different structures ranging from spherical to rod-like. HMS, a type of MSNs, has a unique hollow interior and mesoporous shell, which contribute to its low density, high specific area, and high loading capacity. Various methods can be employed to prepare HMS, including soft templating, hard templating, self-template method, layer-by-layer method, Kirkendall effect, Ostwald ripening, and galvanic replacement.[7]

Mechanism of Formation of MSNs:

A comprehensive comprehension of the process by which MSNs are formed is crucial in order to achieve particles that possess the desired properties for drug delivery. Initial studies on the formation mechanism indicated that the silica network is constructed during the liquid-crystalline phases of non-ionic surfactants. This is particularly evident in materials produced from a diluted surfactant solution, as no evidence of regular mesostructured materials was observed [9]. The literature has demonstrated that the hydrolyzed silica either adsorbs around the micelles or, in the case of SBA-15, the surfactant and silica interact at the early stage and create a core shell-like structure [10]. The formation mechanism of MCM-41 is depicted in Figure.3 Research groups have been diligently working to uncover the precise mechanism behind the formation of MSNs since then.

The formation of MSNs has been investigated using in-situ time-resolved small-angle neutron scattering (SANS). By employing this technique, researchers were able to predict the simultaneous changes occurring during the formation process. It was observed that during the initial hydrolysis (~40 s) of the silica source tetramethyl orthosilicate (TMOS), the silicate ions tend to adsorb around the surfactant micelles as the growth phase progresses. As the charge around the surfactant decreases due to the initial hydrolysis and condensation of the silica precursor, the intermuscular repulsion diminishes, facilitating the further formation of small silica aggregates. After approximately 400 s, the reaction mixture contained well-defined hexagonally ordered mesopores of silica, which was confirmed through transmission electron microscopy (TEM) studies. These findings align with the previously proposed 'current bun model' for the mechanism of MSN formation [11,12]

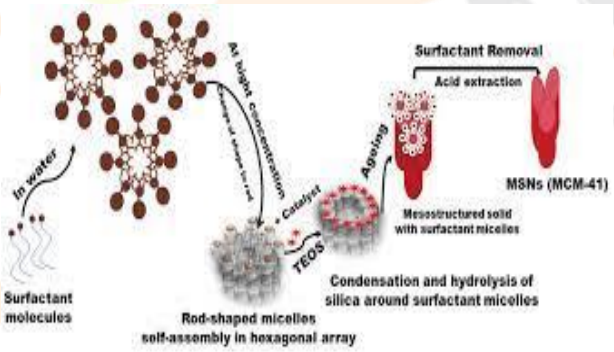

Figure.3 Mechanism of formation of Mobil Crystalline Materials No.41 (MCM-41).

An alternative mechanism called the "swelling-shrinking mechanism" was proposed to explain the formation of MSNs using time-resolved synchrotron small-angle X-ray scattering (SAXS). This mechanism is applicable when only tetraethyl orthosilicate (TEOS) is used as the precursor without any additional solvent like ethanol. When TEOS is used alone, it exhibits phase separation under static conditions, but when vigorously stirred, it forms an emulsion-like system. Initially, cetyltrimethylammonium bromide (CTAB) forms ellipsoidal micelles with a hydrophobic core. When TEOS is added, it dissolves in the hydrophobic core, causing the micelles to enlarge and change from ellipsoidal to spherical shape. Upon hydrolysis of TEOS, the monomers become hydrophilic and are released into the surrounding aqueous environment. The hydrolysed TEOS monomers, which are negatively charged, adsorb onto the positively charged CTAB micelles through electrostatic attraction. As the TEOS within the hydrophobic core is completely consumed, the micelles shrink and decrease in size. Simultaneously, hydrolysis and condensation processes occur, causing the micelles to continuously shrink until all the TEOS is hydrolysed and a silica shell forms around the micelles. The

neighbouring micelles then aggregate, leading to particle growth and the formation of a mesoporous structure [13].

Methods for synthesis of mesoporous silica nanoparticles: -

a) Soft-template method

Different surfactants, such as dual or multi-surfactants, are utilized in order to create a complex template and construct a shell that contains mesopores and hollow inner parts (as depicted in Figure 4).

Figure.4 Synthesis of HMS using soft template method.

In the initial stage, SiO2 is dispersed in an aqueous mixture consisting of lauryl sulfonate betaine and sodium dodecylbenzene sulfonate at a molar ratio of 1:1. Subsequently, in the second stage, 3-aminopropyl trimethoxy silane (APS) is introduced to facilitate the formation of movable core vesicles. Through electrostatic interaction, APS adheres to the surface of these vesicles. The sol-gel transition occurs after the hydrolysis of APS and TEOS, resulting in the formation of layered SiO2 shells. Finally, upon the removal of surfactants, the formation of HMS (hollow mesoporous silica) takes place.[7]

b) Single micelle templating

The conducted an experiment where they utilized Pluronic copolymer with different EO:PO ratios and an organo silica precursor [14]. It was observed that there was no interaction between the micelles and the silicate precursor, as a positively charged surfactant maintained the isolation of the micelle/silica system [15]. Consequently, hollow silica nanoparticles were successfully synthesized through pyrolysis. The technique of single micelle templating resulted in the formation of small hollow mesoporous silica nanoparticles due to the size of the micelles. Typically, the HMS nanoparticles produced using this method have diameters below 20 nm.

c) Vesicle-templating:

It is feasible to enlarge the size of the produced particles through the creation of vesicles. The curvature of mesostructured templates is reduced by the introduction of an anionic surfactant. Hollow mesoporous spheres that have porous shells can directly integrate amino groups. Silica functionalization takes place after the extraction of anionic surfactant with acids [16]. Co-condensation of TEOS and organotriethoxysilanes leads to the formation of uniform HMS. The synthesis yields a solution of triethanolamine and cationic surfactant cetyltrimethylammonium chloride**.**

d) Microemulsion-templating:

The microemulsion method is the preferred choice when the nanoparticles need to be smaller than 100 nm in size. By using a water-in-oil-water emulsion, it is possible to synthesize porous silica nanomaterials with a hollow inner structure. However, completely removing the soft template is a challenging task, often resulting in a reduction in dispersion. The material obtained through the soft templating method typically exhibits an amorphous or semicrystalline phase due to the narrow temperature range used during synthesis. Although high-temperature calcination can eliminate the amorphous phase, it also leads to instability in the mesoporous structure under extreme conditions. To enhance the stability of the particles obtained, the hard template method, also known as the so-called hard template method, has been developed.

e) Hard templating:

Solid templates such as polymer networks, silicate colloids, and metal oxides are utilized in various applications. In order to achieve uniform particles, the silicification process on the organic template's surface must occur at a faster rate than silica self-association. Additionally, the organic template must remain stable during the silica accumulation and condensation process. The frequent interactions between the silicate precursor and the organic template can cause the organic components to be extracted from the solution, making structure formation impossible and leading to synthesis failure. The template must be separable after the silica condensation phase, which can be accomplished through acid dissolution, high-temperature calcination, or extraction. The free volume and surface area of the resulting particles depend on the successful completion of this stage. Microwave-assisted calcination is a method that can remove the organic template in just a few minutes, but it requires specialized equipment.

f) Polymer bead templating:

This method successfully produces small and uniform particles by utilizing polystyrene and polymethacrylate with the assistance of a rigid template. The template can be easily removed after being calcinated at 500ºC. The calcination process must yield a stable structure, clean pores, and a significant number of silanol groups, which are crucial for the preparation of biomedical systems. Although calcination at a high temperature of 500ºC is commonly used, it is a slow method for template removal [17]. As an alternative, rapid calcination has been investigated, where samples undergo short-term intensive calcination with rapid heating [18] Another variation of this method is Microwave-assisted calcination is a technique that enables the rapid removal of the organic template within a matter of minutes, albeit requiring specialized equipment [19].

g) Layer-by-layer method:

Hollow mesoporous silica nanoparticles fabricated using a layer-by-layer approach consist of multiple layers and cavities. The outer shell is reinforced by sequentially adsorbing oppositely charged components onto a negatively charged mesoporous silica sphere template. These components are held together by strong electrostatic forces [20]. The resulting cavity, obtained by removing the mesoporous silica sphere template, serves as the main volume of the capsules where bioactive substances can be encapsulated. In a study conducted by Javier et al, mesoporous silica spheres were exposed to a catalase solution, leading to the immobilization of the enzyme within them. The catalase-loaded mesoporous particles were then coated with three layers of poly (L-lysine)/poly (L-glutamic acid). Subsequently, the porous core was eliminated by treating the particles with a hydrofluoric acid/ammonium fluoride buffer at pH 5 [21]. This process resulted in the formation of hollow mesoporous silica nanoparticles. The layer-by-layer technique offers great versatility, allowing for easy adaptation of the two components to meet specific application requirements.

h) Self-template method:

The self-template method is a technique utilized to synthesize hollow silica nanoparticles without the need for a separate template. In this process, mesoporous silica particles are coated with cationic polydimethyldiallyl ammonium chloride in an alkaline solution, allowing the nanoparticles to be transferred into a cavity structure. Silica oligomers are dissolved by hydroxyl ions, which are negatively charged and subsequently sediment onto the positively charged layer, resulting in the formation of a crosslinked silica shell [22]. To selectively etch the particles, NaOH is employed, leading to the creation of a hollow structure while under the protection of PVP. This approach is referred to as surface-protected etching [23]. Yu et al. developed a method involving acidic and hydrothermal treatment to selectively etch the inner space, thereby transforming silica nanoparticles into hollow structures [24]. Wong et al. successfully transformed solid silica into hollow structures by subjecting them to a 30-minute treatment, during which it was determined that the inner layer possessed a sponge-like structure and could be selectively etched with hot water. The outer layer, on the other hand, exhibited greater rigidity due to the formation of silicic acid aggregates following the Stober reaction. This demonstrates that Stöber silica particles are not homogeneous and that it is indeed possible to produce hollow nanostructures from them using the self-template method [25]. The self-template methods offer advantages in terms of cost and simplicity.

Applications

1) Biological Applications of MSN:

The intravenous injection of MSN at a dosage of 50 mg/kg was found to be well tolerated based on serological, hematological, and histopathological examinations of blood samples and mouse tissues (Lu et al., 2010).

a) Drug Delivery

In terms of drug delivery, early systems utilizing MSNs capitalized on their large surface areas and pore volumes. Guest molecules were simply adsorbed onto the mesopore surface without any gate-like functional group controlling the release of the loaded substances. The release mechanism was governed by either the size or morphology of the pores. Research demonstrated that the MCM-41 type mesoporous structure, characterized by channel-like pores arranged in a hexagonal pattern, could effectively load significant amounts of drug molecules and release them gradually over an extended period. Notably, there were no notable differences observed in the release profiles of materials with varying pore sizes

b) MSN based double drug delivery system

In a study conducted by, it was demonstrated that phenyl boric acid-functionalized MSN can effectively co-deliver insulin and cAMP, allowing for controlled release in response to saccharides. The remarkable biocompatibility, cellular uptake properties, and efficient intracellular release of cAMP establish a solid foundation for future biomedical applications involving in vivo controlled-release. MSN based drug delivery systems have been successfully utilized in delivering various substances such as anticancer drugs, siRNA and DNA constructs, as well as membrane impermeable proteins.

c) Intracellular Delivery of Fluorescent dye.

In 2011, Huichen Guo and colleagues conducted a study on the use of Hollow Mesoporous Silica Nanoparticles (HMSNs) for delivering fluorescent dye into cells. Their findings revealed that these HMSNs, which possess large pores and a high capacity for adsorbing chemicals like Fluorescein isothiocyanate (FITC), could be utilized as a delivery mechanism for controlled release of chemicals within live cells. This discovery

has opened up a wide range of potential applications, including drug storage and release, as well as metabolic manipulation of cells

d) Biosensors:

Igor Slowing have highlighted the significant benefits of micro and mesoporous silica, which include high porosity and optical transparency. The large surface areas and pore volumes of these materials enable the encapsulation and immobilization of a considerable amount of sensing molecules per particle, resulting in fast response times and low detection limits. Additionally, the unique feature of optical transparency allows for optical detection through layers of the material, making it an ideal choice for building biosensors. As a result of these advantages, various types of porous-silica based materials have been utilized in biosensor development.

e) Immobilization of Bioactive Molecules:

The immobilization process proves to be highly effective when the support possesses a large surface area and the pore size is either similar or slightly larger than the biomolecule's diameter. Entrapping the biomolecule within the pores can enhance enzyme activity as it allows the protein to maintain its original structural integrity. However, materials such as MCM-41, SBA-15, SBA-16, and MSU-X, which are synthesized using common ionic and non-ionic surfactants, have mesopore sizes that do not exceed 10 nm. Consequently, these materials cannot be utilized as supports for immobilizing molecules that have dimensions greater than this size.

f) Stationary Phase – High performance liquid chromatography (HPLC):

Mesoporous silicas exhibit intriguing characteristics that make them suitable for use as stationary phases in HPLC. These materials possess a large surface area and an organized porous structure, which contribute to their desirability. Additionally, their chemical and mechanical stability under the conditions of chromatographic operations closely resemble that of precipitated silica. Initially, mesoporous silica, composed of loose particle agglomerates selected through sedimentation, was employed as the first material in HPLC. The efficiency of a particular separation is influenced by the chemical nature of the surface, as well as the morphological and porous properties of the material. To ensure smooth flow of the mobile phase through the column and prevent pressure drop, it is crucial for the particle size of the stationary phase to fall within the range of 3 - 10 mm.

2)Non-Biological Applications of MSN

. Furthermore, MSN also play a significant role in catalysis, separation, refineries, and polymer degradation, apart from their applications in biology.

a) Mesoporous silica in catalysis

Mesoporous materials have emerged as highly promising catalysts due to their large surface area and pore volume. Additionally, they offer the advantage of surface modification and control over pore distribution. The efficient diffusion of molecules through the catalyst pores enables direct interaction with the acidic sites on the wall surface, facilitating various conversions. While mesoporous silica can be utilized in basic catalysis, the majority of applications documented in literature focus on acidic catalysis. This involves incorporating moderate to strong acidic sites into the silica framework. Over the past decade, a significant application has been the use of mesoporous silica as a catalytic support or template for synthesizing carbon nanotubes.

b) Metal Nanoparticles Confined in Mesoporous materials as Catalysts:

According to a study by Sun and Bao (2008), the utilization of supramolecular self-assembled porous materials has introduced a novel approach to incorporate nanoparticles within the channels of these materials. The uniform pore structures of these materials enable the trapped metal nanoparticles to maintain their uniformity even when subjected to high-temperature processes such as activation or pre-treatment. This characteristic is crucial in ensuring their high dispersion and activity retention during catalysis.

c)Molecular Sieves

Mesoporous silica plays a crucial role as molecular sieves in various industries such as petroleum refineries, air separation, and nuclear waste management. According to Michale Tapetis, significant progress in comprehending and regulating their growth, as well as predicting their properties, could potentially facilitate the integration of these materials in thermo electric devices, micro reactors, and as protective coatings against corrosion. However, the production of mesoporous silica and other molecular sieves in large quantities compromises their structural perfection (defect density), uniformity in particle size and shape, external surface perfection, and purity.

d)Refining Industries

Bapan (2003) have stated that mesoporous silica possessing a large pore size can enhance the movement of reactant and product molecules within and outside the pore system. The refining industry necessitates large pore systems for shape selective conversions of bulky molecules, while heavy organics from industrial waste waters require oxidation in such systems. Additionally, the fine chemicals and pharmaceutical manufacturing sectors also benefit from the use of large pore systems.

e) Polymer Degradation

Plastics and polythene are materials that cannot be avoided in our daily lives. While they are commonly used for packaging, storage, and protection purposes, it is important to acknowledge that the accumulation of such materials on the Earth's surface leads to various issues such as soil infertility and the destruction of marine organisms. This is primarily due to their slow biodegradation process. In a study conducted the cracking of HDPE was demonstrated on all-silica MCM-41 materials. The mesoporous silica exhibited a high catalyst activity for cracking, resulting in a fast reaction rate and a different composition of the products compared to reactions without a catalyst. Many researchers have already published the effectiveness of mesoporous silica in HDPE cracking. However, proposed a carbonium ion-mediated mechanism for the cracking reaction. It has been suggested that the cracking of HDPE over all-silica MCM-41 occurs through a free radical mechanism, and the pore structure of the material acts as a reaction vessel, stabilizing the free radicals. Additionally, MSN has been found to be capable of degrading various other polymers.[27]

Current and Future Perspectives:

Although FDA has approved only a few nanomedicines for treatment and use in the clinics, these novel systems have been successful in laying a huge impact in the field of disease therapy and have the potential to change the conventional treatment or diagnosis. Ever since the first identification of the potential application of MSNs as carriers for drug delivery, exhaustive research is being carried out to prove the importance of this technology in the therapy of multiple diseases. Majority of the work focuses on the use of these carriers for site-specific delivery of chemotherapeutic agents. Nonetheless, regulatory and technical obstacles limit the safe and efficient translation and regulatory approval of these products. Unlike other nanocarriers, the fabrication of MSNs is a simple and cost-effective process. Moreover, these MSNs have an additional scope of being a

multifunctional nanocarrier for spatial, temporal placement of drugs and also for theranostic purpose and imaging, and also supports multidrug loading. Remarkable outcomes have been achieved in this regard in both cellular and preclinical studies. However, certain challenges lay ahead in the successful translation of this platform to bedside. Synthesis of MSNs with consistent characteristics and quality can be a major challenge. The industrial transfer of technology mainly depends on scalability and hence the synthesis of MSNs at production scale may be a barrier to its commercialization. There is a need for a better understanding and control of the manufacturing process to ensure reproducibility in the product. In addition, all drugs cannot be loaded in the same concentration and hence the amount of MSN may vary from case to case which may play a role in determining the maximum tolerated dose of MSN. Certain process analytical tools such as custom-built fluorescence correlation spectroscopy (FCS) coupled with size exclusion/gel permeation chromatography (GPC) adopted by Chen et al. would aid in monitoring the particle size and long-term stability and thus reduce batch-to-batch variation. While the inherent toxicity issues of most of the inorganic nanoparticles remains a major issue, encouraging reports on the efficacy and biocompatibility of MSNs in animal models shows the tremendous potential of shifting this platform to clinical levels. However, the difference in the physiology of small animals and humans may lead to failure of these carriers in clinical trials. Lack of in-depth understanding of the interaction between MSNs and the biological system needs to be addressed. Comprehensive in vitro screening assays with varying ligands to ensure optimum uptake, stability, specificity and pharmacokinetic profile would be useful in developing a more reliable product for clinical trials especially for anticancer therapy and the same could be extended as a guide to develop more reliable MSN products for other biomedical purposes as well. Recently, a ray of light for the use of silica nanoparticles was seen in the form of FDA's approval to conduct stage I human clinical trial for Cornell dots (C dots). This marked an important step towards the acceptance of silica nanoparticles. Following this, first-in human studies by Bukara and group demonstrated the safety of MSNs. Nevertheless, the potential challenge to the clinical translation of MSN-based drug delivery system lies in the lack of substantial evidence on its chronic toxicity studies, genotoxicity and teratogenic potential, long-term tissue compatibility. Thorough understanding of the degradation mechanism of mesoporous silica in vivo is yet to be established. Efforts are to be made by researchers like us to bridge the gap between the preclinical and clinical use of MSNs to achieve marked progress in this subject. We anticipate that if a careful assessment during the production and in vitro evaluation along with studies to ascertain the biosafety of MSNs is performed, these novel designs can be a vital breakthrough in the future for clinical applications in the diagnosis, imaging and treatment catering to the needs of patients [2]

Conclusion:

The effective and efficient delivery of drugs to defected cells or tumour cells with minimal toxic side effects is a significant challenge in the field of medicine. This is often due to the lack of specificity and solubility of drug molecules, which necessitates high doses for desired therapeutic effects. To address this issue, various drug carriers have been developed in the pharmaceutical field to aid in the targeted delivery of therapeutic drugs or genes. Among these carriers, mesoporous silica nanoparticles (MSNs) have emerged as biocompatible, chemically and thermally stable nanoparticles with unique structural properties. These properties enable the loading of drugs or genes onto MSNs and their subsequent controlled release at the target site. Over the years, there has been a substantial increase in research on MSNs, starting from the proposal of MCM-41 in 2001, followed by SBA-15 and MCM-48 as drug carriers for controlled delivery systems. The morphological characteristics of MSNs, such as pore size, pore volume, particle size, surface area, pH, and drug loading capacity, greatly influence their performance when modified. Additionally, the functionalization of MSNs using organic and inorganic groups enhances the delivery of drugs to the targeted site. This review article also discusses recent research on the synthesis methods of MSNs and their applications in medicine, imaging, diagnosis, cellular uptake, targeted drug delivery, cell tracing, and bio-sensing.

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