OXFORD JOURNAL
OF STUDENT
SCHOLARSHIP

Recent Synthesis Approaches for Silica Nanoparticles Using the Sol-Gel Method

Taehong Kim[1], Kacey Song[2], Hyoju Kim[3], Gurnho Park[4], Junho Park[5], Ho Yeon Kim[6], Young Bok Kang[7]

taehongkim001@gmail.com, kaceyps08@gmail.com, juliek080909@gmail.com, gurnhopark@gmail.com, leojunhopark@gmail.com, hkim5@loyola.edu

ABSTRACT

The universal and efficient sol-gel method in the synthesis of silica nanoparticles (SNPs) allows for applications in biomedicine, materials science, and environmental engineering. This method is based on liquid precursors, which are converted into solid gels through hydrolysis and condensation, allowing for precise control of the size, shape, and surface properties of nanoparticles. We surveyed recent efforts to improve the sol-gel method that have focused on green synthesis using renewable feedstocks, such as bio-waste materials, and on improving particle homogeneity by optimizing reaction conditions. Additionally, novel methods have been developed to enhance the scalability and mono-dispersity of silica nanoparticles (SNPs) through the use of novel reactor systems, including microfluidic reactors. Along with the great improvement of this process, we also addressed some challenges including reproducibility, control of pore size distribution, particle aggregation, morphology inconsistency, and scaling up for industrial uses. We expect that significant efforts to overcome challenges in the sol-gel method will continue to open up new trends for various applications in developing high-value-added and eco-friendly materials with specific properties and broadening its perspectives in nanotechnology.

INTRODUCTION

Sol-gel is a method for creating inorganic polymers or ceramics from liquid precursors, leading to the formation of a network structure known as a "gel." The sol-gel method consists of four stages–hydrolysis, growth, condensation, and aggregation–describing the transition from liquid precursors to a "sol,"a colloidal suspension, and eventually to a "gel." The sol phase typically involves hydrolysis and condensation of metal alkoxide precursors, resulting in colloidal particles or molecular polymers dispersed in a liquid medium (1). Gelation occurs when these particles destabilize or undergo cross-linking to form a continuous solid network supporting a liquid phase (2, 3). Various factors such as precursor selection, gelation conditions, and processing techniques can be adjusted to control the properties and morphology of the resulting materials (4, 5).

Throughout the article, many related yet not interchangeable materials are mentioned. It is important to distinguish between them, specifically silica nanoparticles, mesoporous silica nanoparticles, silica gels,

thin films, and silica-based membranes. Depending on how the precursor sol is processed, the sol-gel method results in a distinct material structure-wise (1). Silica nanoparticles (SNPs) are solid (non-porous) 0d spheres, and mesoporous silica nanoparticles (MSNs) are 0d spheres that feature an internal pore network, whereas silica gels are a 3D continuous solid network, thin films are a 2D flat surface coating, and silica-based membranes are a either 2D or 3D porous filter layer.

The sol-gel method stands out as a prominent technique in improving existing materials and available nanostructures due to its efficiency and simplicity (6, 7, 8). Additionally, the sol-gel method is commonly used to produce silica particles effectively, as it allows for a synthesis route that is high in purity, uniform, scalable, and controllable (9).

The versatility of the sol-gel method facilitates the production of high-quality materials tailored for diverse applications spanning biomedicine, electronics, and beyond (11).

Silica nanoparticles (SNPs) synthesized via sol-gel are valued in medical, biological, chemical, agricultural, environmental engineering, material sciences, and industrial fields for their low toxicity, chemical stability, optical transparency, and biocompatibility (10). They also serve as effective carriers in the nanomedicine field.

This review highlights the sol-gel methods developed for synthesizing SNPs and their applications. Notably, we address the challenges and limitations that the current sol-gel methods face and provide our perspective for the future trend.

Review Methodology

A literature survey was conducted to find recent research on the synthesis of silica nanoparticles using the sol-gel method. Relevant research articles published from 2009 onward were found utilizing searches conducted using Google Scholar. Studies were selected based on their relevance to silica nanoparticle synthesis using sol-gel-based approaches, emphasizing original research describing improvements in sol-gel synthesis, precursor materials, and resulting properties. Information from the studies was organized in a spreadsheet and compared across studies. The collected information was then analyzed to identify recent developments, common approaches, and challenges in sol-gel synthesis of silica nanoparticles.

CURRENT SOL-GEL METHODS FOR SYNTHESIZING SILICA NANOPARTICLES

General Sol-Gel Approach For Silica Nanoparticle Synthesis

There are multiple different methods applied for synthesis of silica nanomaterials, such as chemical vapor condensation, arc discharge, hydrogen plasma-metal reaction, micro-emulsion, hydrothermal, sol-gel, and laser pyrolysis in the vapor phase (12, 13, 14).

Among them, the sol-gel method is commonly used as a process for synthesizing silica nanoparticles because it is versatile and can synthesize materials at low temperatures (19). In the process of synthesis,

larger amounts of silanol groups generally enhance silica nanoparticle interactions with surface hydroxyl groups and functional groups of organic moieties in inorganic-organic hybrids. Unique characteristics such as its high surface area, biocompatibility, functionalization, and high mechanical and thermal stability makes silica nanoparticles suitable for the preparation of silica-based polymeric nanocomposites (15, 16, 17, 21) (Figure 1). Synthesis parameters such as pH, temperature, and other molecular compounds can impact the characteristics of the resulting product, including morphology, shape, size, homogeneity, and aggregation.

Numerous researchers have made advancements in sol-gel technologies that transform a colloidal solution into a gel-like structure through chemical reactions (18). Hyde et al. demonstrated three different sol-gel methods for colloidal silica synthesis: precipitated silica synthesis, Stöber method synthesis, and biomimetic sol-gel synthesis (23).

First, the precipitated silica synthesis uses sodium silicate sourced from natural sources such as sugar cane bagasse ash. The "precipitated silica" synthesis method requires neutralizing a soluble silicate with an acid. The silicic acid that is formed through this neutralization process is supersaturated in the solution and becomes precipitated (23). HCl and H_2SO_4 are commonly used as the precipitant for the sodium silicate precursor (23, 25, 26, 27).

Joni et al. demonstrated that the optimal conditions for the production of silica nanoparticles were at 25 °C and pH 7 (28). While precipitated silica synthesis is widely used in the silica industry, it offers limited control over the properties of the resulting silica nanoparticles. As a result, some opt for alternative methods, such as sol-gel synthesis, to achieve greater precision (25).

The Stöber technique is a sol-gel method to synthesize silica particles. It relies on basic conditions to induce silica particle formation and can be facilitated in neutral or acidic conditions by using microemulsions or coprecipitation molecules. Reaction parameters such as reaction concentration and temperature are adjusted to create a more uniform silica sphere and stable surface properties. The hydrolysis of tetraethyl orthosilicate (TEOS) and alcohols is followed by condensation. After the condensation of silica, the next steps include stabilization and growth of silica particles, which are then adapted for coating purposes. Gold nanoparticles can be coated with a silica shell without the need for pretreatment of the gold surface in a seeded polymerization technique based on the Stöber method (23, 29, 30, 31).

The biomimetic sol-gel method of synthesis provides a more environmentally friendly way to have control in surface chemistry rather than the current industrial process of silica synthesis. This method mimics the natural biomineralization process by being observed in diatoms and other silica-participating organisms, which regulate the formation of silica structures under mild conditions using organic templates and biomolecules(23). Specifically, several studies have shown that biogenic silica–an amorphous form of silica (SiO_2) produced by diatoms and other silica-forming microorganisms–forms as organic templates and biomolecules within or around these organisms direct and accelerate silica condensation, effectively guiding the growth and solidification of the silica structure (1, 2, 3). Additionally, studies have shown

alternative amine-containing molecules such as polyamines and peptides as candidates for silica precipitation from precursor compounds in vitro. The use of these alternative amine-containing molecules utilizes a biomimetic approach by focusing on conditions mimicking that of natural, biological processes. Industries such as biomedical manufacturing have produced silica-condensing organisms such as sponges to use as organic templates in controlling the growth of silica assemblies (33).

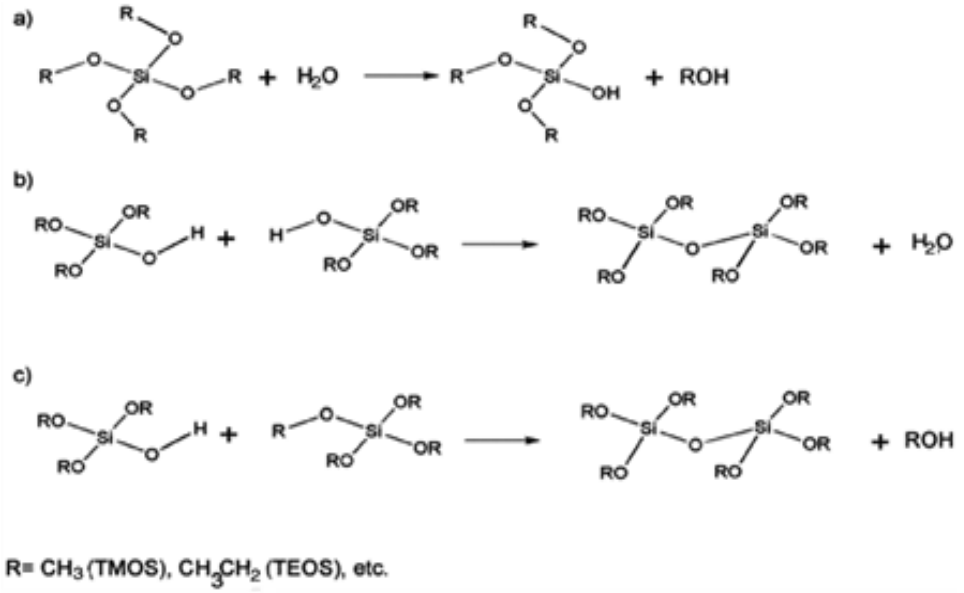

Figure 1. Mechanism of silica gel formation through the sol-gel method. In (a), a tetraalkoxysilane undergoes hydrolysis, forming one or more reactive silanol groups along with alcohol as a byproduct. Two free silanol groups can then condense, resulting in the release of water (b), or a silanol group may react with an alkoxysilane group, leading to the formation of alcohol as a byproduct (c).

Current Sol-Gel Methods

Mesoporous silica materials hold significant promise across various applications, from drug delivery to catalysis, owing to their ordered structure and tunable pore size.

In addition, functionalized silica-based mesoporous materials offer versatile architectures and are key in environmental applications, with co-condensation and post-synthesis methods being the most explored modification strategies. Functionalized silica involves chemically modifying the silica surface to attach specific molecules or groups, altering its properties for targeted applications, while traditional silica refers to its unmodified, natural state (37).

Among the various synthesis techniques for mesoporous silica materials, the sol-gel method has emerged as a versatile method due to its ability to control parameters and low-temperature processing (35). However, traditional sol-gel methods often yield silica nanoparticles with uneven shapes and wide size distributions (38). In a recent study, researchers sought to overcome these limitations by combining traditional sol-gel methods with innovative approaches such as microfluidic reactors. By leveraging a

polydimethylsiloxane microreactor, they created a microfluidic system where reactants were mixed to generate droplets by encapsulating silica nanoparticles with gel solution. This approach allowed the researchers to have precise control over the synthesis process, leading to the production of highly monodispersed silica nanoparticles with a significant reduction in size compared to previous methods. Ultimately, microfluidics improves monodispersity through many factors, such as through controlled mixing and droplet uniformity, which can be executed through the process of micro-mixing. Micro-mixing is affiliated with the micro-droplets, which control the shape and size of the droplet to create more uniform conditions within each droplet. In addition, residence time is another important factor that can affect the monodispersity of silica nanoparticles in microfluidic reactors. Ling et al. demonstrated that residence time can be controlled by changing the flow rate, which changes the size and size distribution of the synthesized silica nanoparticles. The results showed that shorter residence time generally reduced the particle size and size distribution, while longer reaction and aging times can lead to further particle growth and aggregation (85).

Moreover, traditional Stöber synthesis methods encounter challenges like particle aggregation during silica coating. Sharafi et al. demonstrated that combining the Stöber process with sol-gel chemistry and microfluidic reactors offered a promising approach for refining mesoporous silica synthesis (41). Such a modified approach proposes temporarily reducing catalyst concentration to minimize nucleation, then gradually increasing it to promote normal silica formation, thereby preventing aggregation without surface modification. This integrated approach offers precise control over synthesis parameters, enhancing particle monodispersity and preserving silica coating integrity crucial for applications requiring uniform particle dispersion (41).

Likewise, the combination of traditional sol-gel methods with innovative approaches like microfluidic reactors holds immense potential for advancing the synthesis of mesoporous silica materials. By refining synthesis parameters and exploring novel techniques, researchers can unlock new possibilities for applications ranging from drug delivery to energy conversion and storage (18).

Through thermal treatment of rice husk ash utilizing the sol-gel method without additional surfactant, a nano silica powder was obtained and was characterized by various approaches. Similar absorption curves were observed in both standard nanosilica and synthesized nanosilica from the fourier-transform infrared measurements. The nitrogen adsorption-desorption analysis showed that the nano silica particles had a particularly high surface area of 653 m^2/g and a total pore volume of 0.64647 mL/g, but a narrow pore radius of ~1.98 nm. Scanning electron microscopy of nanosilica samples dried at temperatures of 120 °C and 700 °C showed separated particles in the sample dried at 120 °C while the 700 °C sample was aggregated. Transmission electron microscopy (TEM) micrographs showed that 69% of particles ranged in size from 20-25 nm. X-ray diffraction measurements identified the amorphous nature of synthesized silica. The application of the Debye-Scherrer formula provided the corresponding value of mean crystallite size at about 26 nm observed in the TEM (42, 43).

Nano sol-gel with a 5–15 nm pore size has been synthesized recently, where the obtained results indicated that the nano silica powder was successfully prepared via the acid-base route, yielding a predominantly

amorphous mesoporous structure with a high surface area (422 m²/g) (44). In a study, this issue is illustrated in the case of sol-gel derived hierarchically porous and multifunctional silica-based membranes. The impact of the overall porosity and of the pore size distribution on the mechanical properties of these layers was investigated by coupling experimental measurements and numerical simulation (45).

The integration of photocatalysts and biomaterials into sol-gel methods has opened up new avenues for the synthesis of functional materials. By harnessing the principles of sol-gel chemistry, researchers can develop eco-friendly and cost-effective platforms for manufacturing advanced materials with tailored properties (1,4,11,18). Another study demonstrated the potential agricultural application of synthesizing SNPs from barley grass waste, showing that higher temperatures of synthesis enhance the mechanical properties and stability of SNPs, making them suitable for environmentally friendly uses (66). Vashitha et al. demonstrated that SNPs that were synthesized via sodium silicate and sol-gel methods in seawater significantly improved oil recovery by reducing interfacial tension and altering wettability, enhancing final oil recovery by 13.7% in secondary and 8.3% in tertiary recovery (72).

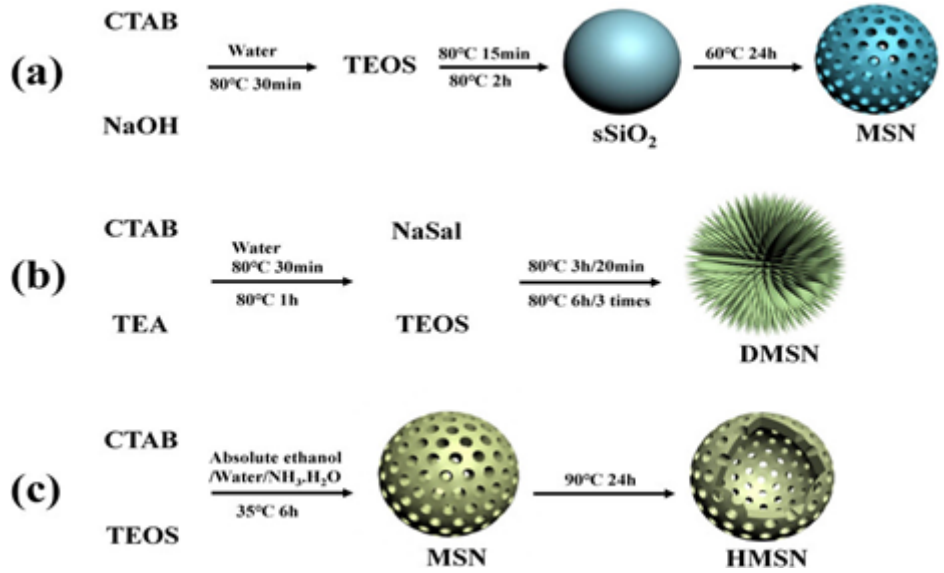

Figure 2. Illustration of several types of nanoparticles. The formations of MSN (mesoporous silica nanoparticles) (a), DMSN (dendritic mesoporous silica nanoparticles) (b), and HMSN (hollow mesoporous silica nanoparticles) (c) are shown above.

The sol-gel method involves various parameters that significantly impact the material's final properties and characteristics, including morphology, shape, size, and homogeneity. These parameters include calcination temperature, aging time, and drying methods, all of which must be carefully controlled to achieve the desired material characteristics.

Researchers have previously examined adjustments such as pH and temperature, as these factors critically influence the hydrolysis and condensation reactions during sol-gel synthesis. Under acidic conditions,

hydrolysis slows down, while basic conditions accelerate it, which directly affects the gel's structure. The temperature is an important factor as well in reaction kinetics and gel formation process. For example, hydrothermal synthesis reaction occurs in alkaline conditions (pH = 13–14) and at temperatures ranging from 90 °C to 200 °C. The sol-gel Pechini method, in particular, offers a controllable approach to synthesizing perovskite nanoparticles, allowing for the manipulation of factors such as precursor composition, pH, working temperature, and reaction time (18).

Synthesizing silica nanoparticles using the sol-gel method emphasizes the role of alcohol solvents in fine-tuning particle size and surface properties (46). Specifically, in the synthesis of nanostructured materials including tetraethyl orthosilicate (TEOS) and titanium isopropoxide using the sol-gel method, metal alkoxides are usually dissolved in a solvent such as water or alcohol and then undergo hydrolysis and condensation reactions to form a sol. These steps determine the final properties of the synthesized material, including its porosity and surface area. Acetic acid and certain surfactants also play significant roles in controlling the gelatin process and the formation of mesoporous structures by influencing the hydrolysis rate (47).

As for other examples, aging times varied between 2 to 6 hours during the synthesis of TEOS-based silica materials. This affected the size and distribution of pores in the final material. Additionally, the drying method determines the mechanical stability and surface area of the final gel. Precise manipulation of these parameters allows for the tailored synthesis of materials with specific applications in fields such as catalysis, drug delivery, and energy storage (14). The sol-gel method utilizing a colloidal solution can be divided into two types: aqueous/hydrolytic and non-aqueous/non-hydrolytic. The use of the sol-gel method across several studies has resulted in various optimized reaction conditions, as each study is different.

Studies describe a method for synthesizing colloidal mesoporous silica nanoparticles with tunable mesopore sizes, ranging from 50 to 300 nm, that exhibit strong adsorption properties. Using swelling agents, the mesopores can be enlarged to 9 nm, allowing the nanoparticles to adsorb significant amounts of biomolecules like hemoglobin and lysozyme quickly, primarily on their external surfaces. These properties make the nanoparticles promising for applications in biomolecule immobilization and adsorption (48).

Mora et al. illustrated that the optimal conditions for synthesizing a silica nanostructure were found to be a calcination temperature of 700 °C and an aging time of 2 hours. TEOS and water were mixed in the molar ratios of H_2O:TEOS = 4:1. Firstly, in this process, TEOS was hydrolyzed to silicic acid. Condensation reactions have led to the formation of Si-O-Si bonds. Core creation is completed after a few hours of the condensation reactions and the layers around the particles continue to be created.

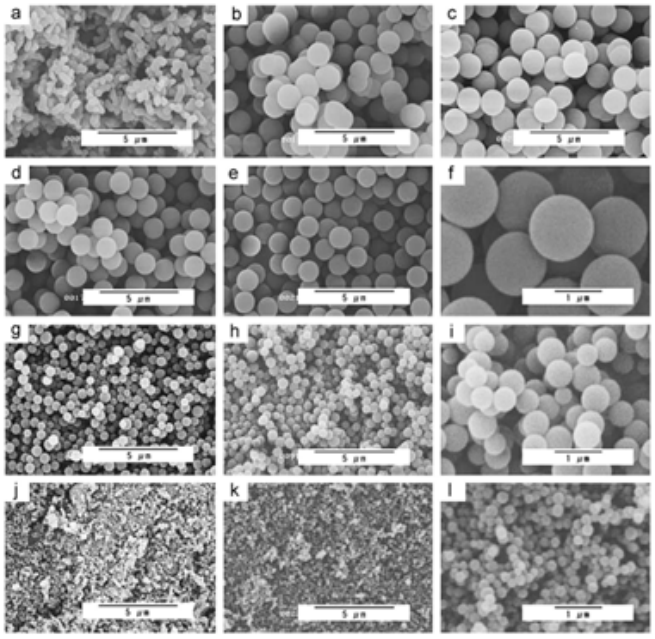

Figure 3. Magnifications of silica nanoparticles synthesized through the Stöber technique. The particle sizes are shown at different magnifications across different methanol to tetraethyl orthosilicate (TEOS) ratios.

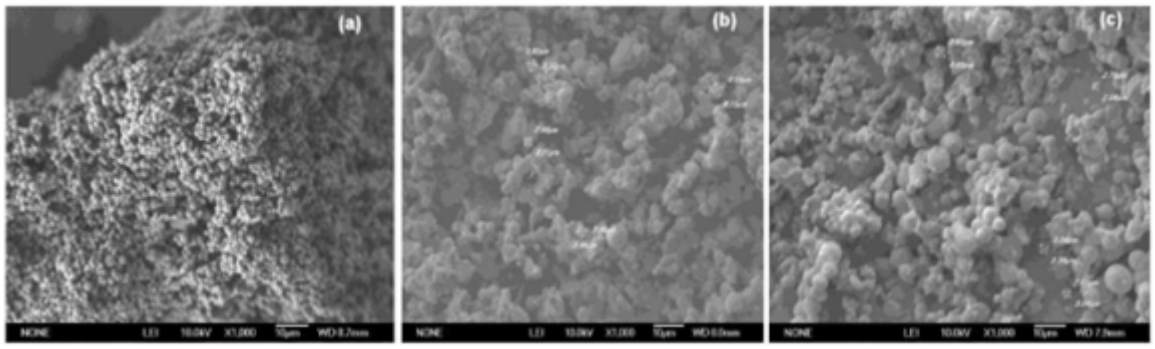

Figure 4. A series of magnified (×1000) silica nanoparticles are shown at various aging times at a calcination temperature of 700℃. The particle sizes of 2 h aged sample ranged from roughly 2.81 μm to 3.29 μm (a), those aged for 4 h ranged approximately from 2.94 μm to 3.29 μm (b), and those at 6 h between 3.14 μm and 3.28 μm (c) (49).

Through the sol-gel synthesis method, Emrie concluded that the optimum temperatures to prepare a good quality silica gel were between 35 °C and 80 °C. The optimal pH for both uniform and ordered mesoporous silica formation is 3. At a pH below 2, silica condensation takes place in the bulk solution, resulting in the formation of silica particles, which hinders the creation of uniform films on the substrate. At a pH close to 4.0, the hydrolysis of TEOS proceeds too slowly to generate enough hydrolyzed silanol for the polycondensation reaction, preventing the formation of mesoporous thin films at this pH. The

surfactant/precursor molar ratio is an important factor to be optimized for the formation of structured and highly ordered mesoporous silica films. They found that the thickness of the mesoporous silica formation is highly dependent on the concentration of the precursor solution. They observed that increasing the alkoxide precursor solution in the range of 50–125 mM while keeping the surfactant/precursor ratio to 0.32, results in a linear increase of film thickness without the formation of aggregates (38).

In Hessien's study, the data suggested that the optimum conditions were measured to be at 110 °C with a 6-hour drying and aging time. The dissolution of 1 mole of tetraethoxysilane (TEOS) in a solvent mixture of 10 mL of ethanol and 35 mL of deionized water was chosen to optimize the hydrolysis and condensation of TEOS. An HCl catalyst (one mole) is added to the mixture to accelerate hydrolysis and then stirred magnetically for 50 min at temperature 60 °C. The solution sits for 2 hours at room temperature for gel formation. After drying the suspension at 110 °C for 6 hours, crystalline SiO_2 particles were formed (50). Overall, such optimized reaction conditions cannot be shortened to a specified temperature or requirement with the varieties of methods used.

Studies following colloidal silica particles have attracted attention from scientists from varieties of fields as the Stöber process synthesized monodisperse spherical silica through hydrolysis of alkoxysilanes in alcoholic solutions. Research has been conducted on dynamic light scattering and was employed to monitor the growth of silica particles. Materials such as those vacuum-distilled with CaO before use, 25% ammonia solution, and absolute ethanol with further purification have been mixed with colloidal silica particles. In the end, the optimized results showed that better monodispersity was achieved with a lower concentration of NH3 and elevated temperatures. Results showed that the growth of the silica seeds finished in an hour and shrank in several nanometers in the following hour.

The drying process in the preparation of nanoparticulate materials and films is a critical step that can significantly affect the final properties of the product. Different drying techniques can be employed to modify surface properties and ensure the stability and integrity of the material. There are different ways of drying, which include supercritical drying conditions, spray drying, freeze drying, etc. (51).

When using a peptised sol—a stabilized colloidal suspension where nanoparticles are dispersed by peptizing agents such as acids, bases, or surfactants—for creating nanoparticle films, it is important to make certain that by-products do not interfere with the application, and the pH is regulated to prevent destabilization of particles. To maintain the nanoparticles' properties, specific procedures are followed to obtain the dry material and remove the by-products. The most important methods for manufacturing films and coatings from sol-gel solutions are dip-coating, spin-coating, and electrophoretic deposition (EPD). Each method requires a careful drying post-deposition, where controlling the atmosphere, humidity, and temperature is essential to avoid cracking (51). The manuscript emphasizes the importance of maintaining sol stability during gelation such as using supercritical drying to preserve pore structures in mesoporous silica nanoparticles or slow evaporation to minimize aggregation in films derived from peptised sols.

During the drying of wet gels, which involves the desorption of water and solvents, the material shrinks and hardens. This step includes interactions of three processes, which are evaporation, shrinkage, and

fluid flow through pore channels. The gel typically cracks due to heterogeneities in the composition or porosity, temperature gradients, or different local reaction rates. To decrease cracking, drying should be performed at slower rates, under a controlled atmosphere or under supercritical conditions (51).

Comparative Summary of Sol-Gel Approaches for Silica Nanoparticle Synthesis

The table below organizes the sol-gel approaches discussed in Section 2 by the precursor/catalyst, pH, temperature, and particle or pore size reported for each. It also lists the advantages and limitations reported in the study so the readers can compare approaches directly

Approach	Precursor / Catalyst	pH	Temperature	Particle / Pore Size	Advantages	Limitations
Precipitated silica (Joni et al.)	Sodium silicate; HCl or H2SO4 precipitant	7 (optimal)	25 °C (optimal)	Not specified in source	Simple, scalable, widely used industrially	Limited control over resulting particle properties
Stöber synthesis	TEOS + alcohol; ammonia (basic conditions)	Basic	Room temperature (variable)	Tunable via TEOS:alcohol ratio	Uniform spherical particles; suitable for silica-shell coatings	Prone to particle aggregation during coating unless modified
Biomimetic sol-gel	Organic templates/biomolecules (e.g., polyamines, peptides)	Mild / near-neutral	Mild (ambient)	Not specified in source	Environmentally friendly; enables surface-chemistry control under mild conditions	Less industrially established; mechanisms less standardized
Microfluidic-reactor-assisted sol-gel	TEOS-based sol in PDMS droplet microreactor	Not specified	Not specified	Significant size reduction; highly monodispersed	High monodispersity via controlled mixing, droplet uniformity, and	Requires specialized microreactor equipment

					residence-time control	
Stöber–microfluidic hybrid, staged catalyst (Sharafi et al.)	TEOS (Stöber) with staged catalyst concentration	Not specified	Not specified	Not specified	Prevents aggregation without added surface modification; preserves coating integrity	Requires precise staged control of catalyst concentration
Rice husk ash-derived silica (thermal treatment)	Rice husk ash (bio-waste); no surfactant	Not specified	Dried at 120 °C or 700 °C	Surface area 653 m²/g; pore volume 0.646 mL/g; pore radius ~1.98 nm; 69% of particles 20–25 nm (TEM)	Green, waste-derived feedstock; high surface area	Narrow pore radius; particles aggregate at higher drying temperature (700 °C)
Acid–base route mesoporous silica	Not fully specified in source	Acid–base route	Not specified	Pore size 5–15 nm; surface area 422 m²/g	High surface area, predominantly amorphous mesoporous structure	Precursor/process details not fully specified in source
TEOS sol-gel, calcination-optimized (Mora et al.)	TEOS; H2O:TEOS = 4:1 (molar)	Not specified	Calcination 700 °C; aging 2 h (optimal)	~2.8–3.3 µm, varies with aging time	Identifies optimal calcination/aging conditions	Resulting particles are micron-, not nano-, scale
TEOS sol-gel mesoporous thin films (Emrie)	TEOS; alkoxide precursor 50–125 mM	Optimal pH 3	35–80 °C (optimal)	Film thickness scales linearly with	Produces ordered, uniform mesoporous thin films	Narrow pH window (pH<2 causes bulk precipitatio

				precursor concentration		n; pH≈4 too slow)
TEOS sol-gel, HCl-catalyzed (Hessien)	TEOS (1 mol) in ethanol/water; HCl catalyst (1 mol)	Acidic (HCl)	60 °C stirring; 110 °C drying	Crystalline SiO2 particles; size not specified	Well-defined stepwise protocol; optimized drying/aging time (6 h) identified	Multi-step, time-intensive process

APPLICATIONS OF SILICA NANOPARTICLES SYNTHESIZED THROUGH THE SOL-GEL METHODS

Biomedical Applications

SNPs synthesized through the sol-gel method hold high potential in biomedical applications due to their biological compatibility as non-toxic particles, tunable surface properties, and controlled release capabilities (27). Specifically, they have been used as scaffolds for regenerating tissue, biosensors for disease detection, and carrying gene and cell therapies (22, 58, 55). Several other factors such as managing their toxicity, degradation behavior, dose dependence, and regulatory barriers directly determine whether SNPs can achieve high potential. Tuning particle properties controls the dose-dependent toxicity, and standardizing quantitative measurements help avoid regulatory barriers (86, 87). The most promising application of colloidal mesoporous silica nanoparticles (MSNs) is in the nanomedicine field, where they serve as effective carriers for drugs, DNA, and proteins. Aughenbaugh et al. (2001) studied the release of drugs and the impact of SiO_2 xerogels as carriers. It was concluded that hydrophobic drugs are less efficient because of their poor water solubility, which leads to lower rates of adsorption during oral dosing. The silica nanoparticles' ability to capture the drug amplifies the overall drug adsorption and reduces the danger posed by the free drug within the body (57). When transporting drugs, mesoporous silica nanoparticles' (MSNs) suitability ensures its place in drug delivery due to its supramolecular nano valves that result in physiological pH (7.4). While some have criticized MSNs for their perceived lack of stability in water and other reactive conditions, this apparent weakness is actually a significant advantage. This is because under physiological conditions, MSNs degrade shortly after delivering the drug or cargo, making them suitable for targeted and controlled release applications in addition to protection against poisoning by acting as catalysts of long operating times (59).

Furthermore, silica nanoparticles play an important role in the use of enzymes in drug discovery and food chemistry. For instance, it has been used to immobilize lipase, enhancing its stability and reusability in industrial food processing and biodiesel production (6). Enzyme activity is a main concern in biochemical studies and it plays an important role in the use of enzymes in drug discovery, food chemistry, and biofuels from enzymatic biomass processing. The hydrolysis and formation of esters catalyzed by lipase

are research topics in organic biosynthesis (57). The immobilization of the enzymes on the nanoparticles is also a focused field currently in nanotechnology. Silica particles with a specific chemical or enzymatic trigger for drug release are particularly beneficial when the exact location of diseased tissue is known and can be targeted by an external energy source. This approach enhances the effectiveness of drug delivery and treatment (53) since MSNs have been explored to deliver various drugs that could treat cancer, bone disorders, and diseases.

Silica nanoparticles have also demonstrated potential for use in various imaging technologies such as forming thin films and polymer composite films due to its colloidal stability and microporosity They are well-tolerated in the body, require small amounts to enhance image contrast, and have the potential for commercial development as imaging contrast agents. The acceptable risk for imaging agents is lower than therapeutic treatments due to their diagnostic or prognostic purpose (59). Additionally, silica nanoparticles have been used to enhance seed viability in plants (e.g. a maize plant) due to their smaller size and their non-toxic nature, surface area and greater absorption capacity by the plant cells (56).

Surface modification offers the potential to incorporate nanostructured silica with polymers or proteins, paving the way for medical applications including dental filling composites, cancer treatment, and drug delivery systems (60, 61). The investigation constructed by Wei Zhang and Manoj Sharma presented a novel gold nanoparticle-capped mesoporous silica nanosphere (PR-AuNPs-MSN) platform tailored for the photoinduced, regulated discharge of the anticancer agent paclitaxel in human fibroblast and liver cells. This system effectively safeguards against premature drug release, thereby ensuring the containment of the cytotoxic agent within live cells. The release of the drug can be meticulously managed through low-power photoirradiation under biocompatible circumstances, thus establishing the potential of this approach for chemotherapy (62). This methodology holds significant promise for the advancement of novel drug delivery systems targeting a variety of hydrophobic toxic agents (63).

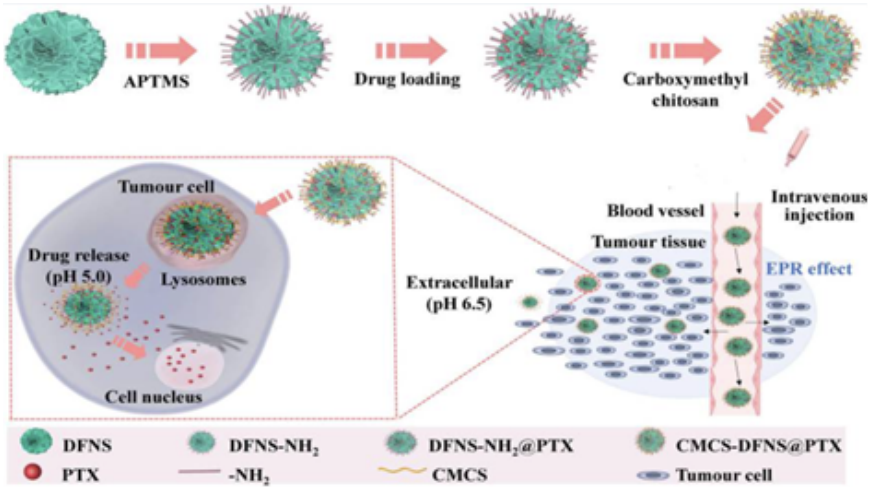

Figure 5. An application of dendritic fibrous nano-silica (DFNS) as a drug delivery vehicle. Carboxymethyl chitosan (CMCS)-functionalized dendritic fibrous nano-silica (DFNS), a silica-based

system, enhances drug absorption in breast cancer cells and improves paclitaxel's effectiveness by extending its circulation time (60).

Agricultural Applications

Agricultural Plant Protection

Akhter demonstrated that hydrophobic silica nanoparticles (SNPs) enhance fungal resistance in maize by activating defensive enzymes and biochemical components, which protect against pre- and post-harvest infections (68). Nanosilica treatment promotes the expression of stress-responsive compounds in maize, enhancing biocontrol activity, particularly at dosages of 10–15 kg/ha. The results confirmed that properly functionalized SNPs can effectively reduce the need for chemical fungicides by improving the plant's natural defenses, especially against Fusarium oxysporum and Aspergillus niger. This research paves the way for further genetic studies and applications in plant defense mechanisms (56). The toxicological behavior of SNPs in maize was also studied (Zea mays L.) (65).

Wastewater and Environmental Remediation

Akhayere demonstrated that silica nanoparticles derived from barley grass waste are environmentally friendly when synthesized at high temperature. There were various methods used, such as X-ray diffraction (XRD), scanning electron microscopy (SEM), energy-dispersive X-ray (EDX) analysis, Brunauer-Emmett-Teller (BET), Fourier transform infrared (FTIR) and X-ray fluorescence (XRF) spectrometry analysis.This allows the nanosilica particles to be collected from the barley and applied as absorbents in wastewater cleaning, leveraging their favorable properties. This wastewater cleaning can help address water pollution over the long term, eliminate potentially harmful bacteria in crop, and support a healthier environment overall (26).

Food and Packaging Applications

Peters illustrated that silica is often used as an application in the food industry, specifically to produce a thicker texture and more flavorful product. When food containing low levels of nano-sized silica is consumed, previously existing low pH levels have been shown to become neutral with the help of silica particles. Highly concentrated silica nanoparticles have been provided to humans in the form of plant-derived foods as a food additive. Overall, silica nanoparticles benefit the agricultural industry by helping it provide a wider variety of nourishing foods (24).

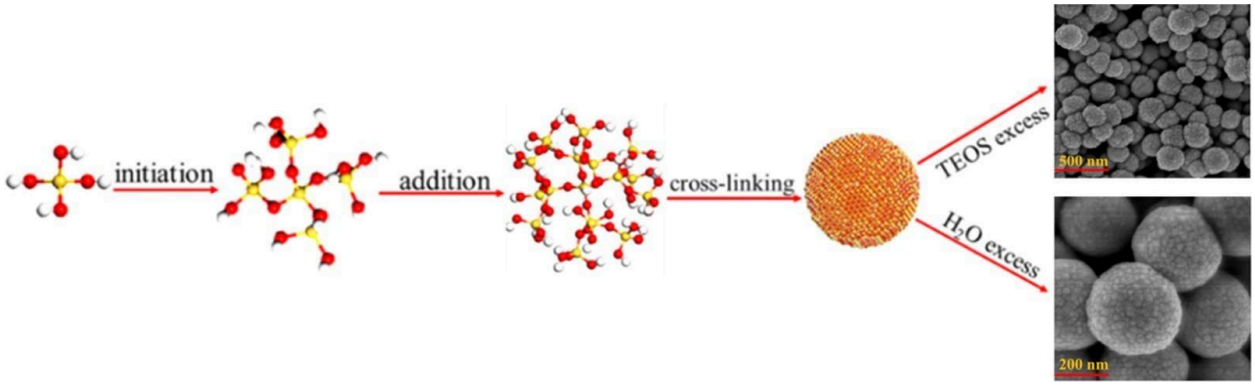

Figure 6. Formation of silica nanoparticles through a sol-gel process. The nano-silica particle size is enlarged by increasing concentrations of H_2O and TEOS in ethanol. The process details the initiation, addition, and cross-linking of the nanoparticles, with the H_2O forming smooth surfaces while those treated with TEOS had rough, poor surfaces.

Silica also plays a vital role as ingredients in food, pesticides, and personal care products; as fillers in plastics, rubbers, and coatings; and as starting materials for semiconductors, silicates, and ceramics. This allows it to provide the benefit by the way it is obtained regardless of the final chemical composition of the material (4). There are numerous nanomaterials that can be used for various food packaging applications on an industrial scale. As for fields like chemistry, the sol-gel method provides scientists with advantages in controlling the reaction when synthesizing solids, which allows them to determine the properties of the resulting material.

Other Industrial Applications

Hydrophobic silica nanoparticles (SNPs) and thin-film coatings offer promising advancements for future technologies and methods.

Thin-film coatings—comprising materials like TiO2, SiO_2, MgF2, gold, and aluminum—applied to surfaces such as metal, crystals, glass, or ceramics, alter optical properties to produce effects like reflection, refraction, conductivity, and anti-reflection. These coatings are essential in many high-tech devices, such as flat-panel TV screens, solar cells, spectacle lenses, and smartphones. By precisely controlling the optical properties of surfaces, thin-film coatings enhance energy efficiency, visibility, and durability, driving innovation and improving the functionality of a wide range of high-tech devices and materials (69).

SNPs created through the sol-gel method are also used in the tire industry to reinforce the rubber compounds and improve tire properties; one study explored the use of vinyl-based silica nanoparticles to improve non-agglomeration and dispersion of the nanoparticles throughout the rubbery material (70).

Thin-film coatings play an important role in enhancing the efficiency of solar cells by optimizing light absorption and conductivity. Integrating nanostructured and multi-layer thin films presents better

opportunities for next-generation solar cells through improvements in light trapping, self-cleaning properties, and stability under harsh environmental conditions.

CHALLENGES AND FUTURE PROSPECTS

Limitations and Challenges

The sol-gel method, despite its numerous advantages, faces several limitations that hinder the improvement of the synthesis of silica nanoparticles. Controlling pore size and pore distribution, and achieving uniformity in the final product, can be difficult, impacting the material's performance. The process often struggles to form highly ordered structures consistently and maintaining stability during synthesis is complex (69). Increasing surface area without compromising other properties is challenging, and the high sensitivity to processing conditions can lead to reproducibility issues.

Specific disadvantages include difficulty in controlling particle size, longer reaction times, and the high sensitivity to minor variations in conditions. Toxicity, the cost of precursors, moisture sensitivity, and the complexity of scaling up production further complicate the process (38). The synthesis of SNPs from sodium silicate solution via sol-gel in alkaline medium is less explored, with challenges in controlling nanoparticle size and preventing agglomeration (74). However, it was found that the size of colloidal silica could be adjusted by varying the temperature, titration rate, and potassium hydroxide concentration.

Additionally, during processing, significant dimensional changes of SNPs may lead to high permeability, low wear-resistance, weak bonding, and difficult porosity control that limit the material's durability and functionality. The process also suffers from a maximum coating thickness limit, thermal mismatch issues, and costly raw materials and processing steps (69). Alkoxide-based sol-gel chemistry specifically faces challenges with shaping and stability of metal alkoxides and moisture sensitivity (1). Overall, overcoming these limitations requires further research and development to enhance control, reduce costs, and improve the stability and reproducibility of sol-gel materials.

Future Prospects

Current research on silica highlights the versatility of silica nanoparticles synthesized via the sol-gel method, which are valued for their tunable size, shape, and surface properties. These nanoparticles can be applied in biomedicine, environmental engineering, and material sciences due to their unique property of being biocompatible, chemically stable, and nontoxic. However, there is much more to be found and applied in the field of sol-gel chemistry. There is certainly more to discover about the solution state and how molecular interactions and phase separation differ during the gelation process of forming a gel; cost-effective sol-gel processes for synthesizing novel materials that can propel nanoscale photovoltaic technology forward, offering innovative solutions to the global energy crisis; and reaction parameters like pH, temperature, and pressure during synthesis that could possibly be fine-tuned to produce nanostructures with specific, desired properties. Researchers have made significant efforts to optimize sol-gel synthesis conditions, focusing on fine-tuning parameters like pH, temperature, and pressure. These adjustments have been shown to produce nanostructures with improved stability, efficiency, and scalability, which are crucial for advancing photovoltaic technologies. Advances in these areas could lead

to more cost-effective and sustainable methods for producing nanomaterials, addressing key challenges in energy applications and contributing to solutions for the global energy crisis (75).

A challenging aspect that can be researched in the future is the synthesis of mesoporous phosphate-based materials using the sol-gel route. This difficulty likely results from a narrow processing window, occurring between the departure of organics from the structure and the temperature at which the glass softens and collapses. Addressing this challenge will require a deeper understanding of the underlying reaction mechanisms and precise control of processing parameters of the reaction, such as temperature gradients, catalyst selection, and the inclusion of stabilizing agents. (4).

Creating novel materials through simple, affordable sol-gel processing offers a advantage for advancing nanoscale photovoltaic technology to the next level, which could help address the energy crisis worldwide. For example, sol-gel processing can create a perovskite oxide thin film of solar cells. Due to its low-cost precursors, this method can eventually improve the solar cells and eventually contribute to making energy that is more affordable and accessible, potentially solving the energy crisis worldwide.

When producing various nanostructures with certain properties, reaction parameters including pH, reaction time, temperature, and pressure during synthesis can be adjusted to attain novel nanostructures. Apart from their useful applications, it is essential to monitor and minimize the environmental hazards arising from the reaction by-products, including those associated with mesoporous organosilica nanoparticles (MONPs) (76).

The sol-gel method provides a rare opportunity to create porous glass-based materials with tunable porosity under specific synthesis conditions parameters that impact the hydrolysis and condensation reactions when properly controlled. In addition, the low-temperature sol-gel synthesis offers the possibility of incorporating materials that would otherwise degrade at higher temperatures (77).

We expect that significant efforts to overcome challenges in the sol-gel method will open up new trends for various applications in developing high-value-added and eco-friendly materials with specific properties, further broadening its perspectives in nanotechnology, and exploring their biomedical uses (54).

CONCLUSION

We outlined the trend of the sol-gel methods to synthesize silica nanoparticles in the recent decade. The sol-gel method is proven to be extremely versatile in synthesizing silica nanoparticles due to their simplicity and ability to incorporate a variety of components and use renewable resources. Recent developments have especially focused on the use of renewable and waste-derived precursor materials, microfluidic control during particle synthesis, optimization of pore size and morphology, and surface functionalization depending on the specific application. This adaptability allows for a wide variety of materials with customized properties, highlighting sol-gel's effectiveness. Moreover, the diverse types of gels and nanoparticles produced through the sol-gel process offer various applications across a variety of

fields, including biomedicine and materials science. However, reproducibility, control of particle and pore properties, and scaling up the synthesis process for industrial uses still remain as important challenges. We conclude with a discussion of the limitations and challenges in the current development of the sol-gel method for the synthesis of SNPs, but remain optimistic for future perspectives. As this area of research expands, sol-gel will prove to be a sustainable approach to material synthesis and application.

ACKNOWLEDGEMENTS

Thank you to Sophia Lee for her mentorship in writing this review paper

AUTHOR INFORMATION

[1]Taehong Kim
American Heritage School Broward Campus, 12200 W Broward Blvd, Plantation, FL 33325, USA
Grade 12
taehongkim001@gmail.com

[2]Kacey Song
Coppell High School, 185 W Parkway Blvd, Coppell, TX 75019, USA
Grade 12
kaceyps08@gmail.com

[3]Hyoju Kim
Lone Star High School, 2606 Panther Creek Pkwy, Frisco, TX 75033
Grade 12
juliek080909@gmail.com

[4]Gurnho Park
Canyon Crest Academy, 5951 Village Center Loop Rd., San Diego, CA 92130, USA
Grade 12
gurnhopark@gmail.com

[5]Junho Park
Canyon Crest Academy, 5951 Village Center Loop Rd., San Diego, CA 92130, USA
Grade 10
leojunhopark@gmail.com

[6]Ho Yeon Kim
Loyola University Maryland, 4501 N Charles St, Baltimore, MD 21210, USA
Professor (Mentor)
hkim5@loyola.edu

[7]Young Bok Kang
Georgefox University, 414 N. Meridian St Newberg, OR 97132, USA
Professor (Mentor)

REFERENCES

1. Danks, A.E.; Hall, S.R.; Schnepp, Z. The evolution of 'sol–gel' chemistry as a technique for materials synthesis. Mater. Horiz. 2016, 3, 91–112.

2. Katoueizadeh, E.; Rasouli, M.; Zebarjad, S.M. A comprehensive study on the gelation process of silica gels from sodium silicate. J. of Mater. Res. and Tech. 2020, 9, 10157-10165.

3. Huang, Y.; Li, P.; Zhao, R.; Zhao, L.; Liu, J.; Peng, S.; Fu, X.; Wang, X.; Luo, R.; Wang, R.; Zhang, Z. Silica nanoparticles: Biomedical applications and toxicity. Biomed. Pharmacother. 2022, 151, 113053.

4. Owens, G.J.; Singh, R.K.; Foroutan, F.; Alqaysi, M.; Han, C.-M.; Mahapatra, C.; Kim, H.-W.; Knowles, J.C. Sol–gel based materials for biomedical applications. Prog. Mater. Sci. 2016, 77, 1–79.

5. Bokov, Dmitry, Turki Jalil, Abduladheem, Chupradit, Supat, Suksatan, Wanich, Javed Ansari, Mohammad, Shewael, Iman H., Valiev, Gabdrakhman H., Kianfar, Ehsan, Nanomaterial by Sol-Gel Method: Synthesis and Application, Advances in Materials Science and Engineering, 2021, 5102014, 21 pages, 2021. https://doi.org/10.1155/2021/5102014

6. Zarkov, A. Sol–Gel Technology Applied to Materials Science: Synthesis, Characterization and Applications. Materials. 2024, 17(2), 462.

7. Navid Y.; Olatunji O.; Boyun G.; Ning L. A comprehensive review on the loss of wellbore integrity due to cement failure and available remedial methods. Journal of Petroleum Science and Engineering. 2021, 207, 109123.

8. Tsai, J., Sun, C., Lin, J., Lu, X.-C., & Huang, S.-H. (2022). Magnetic properties and microstructure of FePt (Ag, C) films with MgTiOBN/CrRu underlayer. Surface and Coatings Technology, 436, 128136. https://doi.org/10.1016/j.surfcoat.2022.128136

9. Ismail, A.; Widyaningtyas, A. L.; Susanto, B. H.; Nasikin, M. Facile Synthesis Silica Nanoparticles from Indonesia Silica Sand and their Physico-Chemical Properties. Key Eng. Mater. 2020, 862, 35–39.

10. Gubala, V.; Giovannini, G.; Kunc, F.; Monopoli, M. P.; Moore, C. J. Dye-doped silica nanoparticles: synthesis, surface chemistry and bioapplications. Cancer Nanotechnol. 2020, 11, 1.

11. Zanotti, K.; Igal, K.; Colombo Migliorero, M. B.; Zuin, V. G.; Vázquez, P. G. Synthesis of Silica-Based Materials Using Bio-Residues through the Sol-Gel Technique. Sustain. Chem. 2021, 2 (4), 670–685.

12. Su, X.; Li, H.; Lai, X.; Zhang, L.; Wang, J.; Liao, X.; Zeng, X. Vapor-Liquid Sol-Gel Approach to Fabricating Highly Durable and Robust Superhydrophobic Polydimethylsiloxane@Silica Surface on Polyester Textile for Oil-Water Separation. ACS Applied Materials & Interfaces. 2017, 9 (33), 28089-28099.

13. Jamkhande, P.G.; Ghule, N.W.; Bamer, A.H.; Kalaskar, M.G. Metal nanoparticles synthesis: An overview on methods of preparation, advantages and disadvantages, and applications. J. of Drug Deliv. Sci. and Tech. 2019, 101174.

14. Azlina, H. N.; Hasnidawani, J. N.; Norita, H.; Surip, S. N. Synthesis of SiO2 Nanostructures Using Sol-Gel Method. Acta Phys. Pol. A. 2016, 129, 842–849.

15. Florensa, M.; Llenas, M.; Medina-Gutiérrez, E.; Sandoval, S.; & Tobías-Rossell, G. Key Parameters for the Rational Design, Synthesis, and Functionalization of Biocompatible Mesoporous Silica Nanoparticles. Pharmaceutics. 2022. 14. 2703.

16. Shange, M. G., Khumalo, N. L., Mohomane, S. M., & Motaung, T. E. (2024). Factors Affecting Silica/Cellulose Nanocomposite Prepared via the Sol–Gel Technique: A Review. Materials, 17(9), 1937. https://doi.org/10.3390/ma17091937

17. Budnak, T.M.; Pylypchuk, I.V.; Tertykh, V.A.; Yanovska, E.S.; Kolodynska, D. Synthesis and adsorption properties of chitosan-silica nanocomposite prepared by sol-gel method. Nanoscale Res. Lett. 2015, 10, 87.

18. Navas, D.; Fuentes, S.; Castro-Alvarez, A.; Chavez-Angle, E. Review on Sol-Gel Synthesis of Perovskite and Oxide Nanomaterials. Gels. 2021, 7, 275.

19. Karimzadeh, I.; Aghazadeh, M.; Doroudi, T. Green Synthesis of Silica Nanoparticles via Sol-Gel: Low-Temperature Routes and Biomedical Applications. Mater. Chem. Phys. 2024, 129012. https://doi.org/10.1016/j.matchemphys.2024.129012.

20. Fuertes, A.B.; Vigón, P.V.; Sevilla, M. Synthesis of colloidal silica nanoparticles of a tunable mesopore size and their application to the adsorption of biomolecules. J. Colloid Interface Sci. 2010, 349, 173-180.

21. Yosff, S.N.H.M.; Ramli, H.; Zainal, N.; Halim, S.I.A.; Chan, C.H. 4 - Thermoplastic-based polymer blend nanocomposites for energy storage. Polym. Blend Nanocompos. Energy Storage Appl. 2023, 109-160.

22. Chiavaioli, F.; Biswas, P.; Trono, C.; Jana, S.; Bandyopadhyay, S.; Basumallick, N.; Giannetti, A.; Tombelli, S.; Bera, S.; Mallick, A. Sol-Gel-Based Titania-Silica Thin Film Overlay for Long Period Fiber Grating-Based Biosensors. Anal. Chem. 2015, 87, 12024-12031.

23. Hyde, E.D.E.R,; Seyfaee, A.; Neville, F.; Moreno-Atanasio, R. Colloidal Silica Particle Synthesis and Future Industrial Manufacturing Pathways: A Review. Ind. Eng. Chem. Res. 2016, 55, 8891-8913.

24. Peters, R.; Kramer, E.; Oomen, A. G.; Rivera, Z. E. H.; Oegema, G.; Tromp, P. C.; Fokkink, R.; Rietveld, A.; Marvin, H. J. P.; Weigel, S.; Peijnenburg, A. A. C. M.; Bouwmeester, H. Presence of Nano-Sized Silica during In Vitro Digestion of Foods Containing Silica as a Food Additive. *ACS Nano* 2012, 6(3), 2441–2451.

25. Joni, I.M.; Rukiah; Panatarani, C. Synthesis of Silica Particles by Precipitation Method of Sodium Silicate: Effect of Temperature, pH and Mixing Technique. AIP Conf. Proc. 2020, 2219, 080018.

26. Megawati M.; Fardyanti D.S.; Putri, R.D.A.; Fianti, O. Synthesis of Silica Powder from Sugar Cane Bagasse Ash and Its Application as Absorbent in Adsorptive- distillation of Ethanol-water Solution. MATEC Web Conf. 2018, 237, 02002.

27. Watanabe, Y; Amitani, N; Yokoyama, T. Synthesis of mesoporous silica from geothermal water. Scientific reports. 2021, 23811.

28. Klapiszewski, L.; Królak M; Jesionowsk K. Silica synthesis by the sol-gel method and its use in the preparation of multifunctional biocomposites. Versita. 2013, 12, 173-183.

29. Ghimire, P; Jaroniec, M. Renaissance of Stober method for synthesis of colloidal particles: New developments and opportunities. Elsevier. 2021, 584, 838-866.

30. Zhang, L.; Wan, Y.; Zhao, D. Anionic Surfactant-Templated Synthesis of Ultrahigh-Surface-Area Mesoporous Silica Nanoparticles for Catalytic and Adsorption Applications. Microporous Mesoporous Mater. 2024, 365, 112876. https://doi.org/10.1016/j.micromeso. 2024. 112876.

31. Ghodrati, M.; Mousavi-Kamazani, M.; Bahrami, Z. Synthesis of superhydrophobic coatings based on silica nanostructure modified with organosilane compounds by sol–gel method for glass surfaces. Sci. Rep. 2023, 13, 548.

32. Liberman, A.; Mendez, N.; Trogler, W. C.; Kummel, A. C. Synthesis and surface functionalization of silica nanoparticles for nanomedicine. Surf. Sci. Rep. 2014, 69, 132–158.

33. Lei, Q.; Guo, J.; Noureddine, A.; Wang, A.; Wuttke, S.; Brinker, C. J.; Zhu, W. Sol–Gel-Based Advanced Porous Silica Materials for Biomedical Applications. Adv. Funct. Mater. 2020, 30, 1909539.

34. Ab Rahman, I.; Padavettan, V. Synthesis of Silica Nanoparticles by Sol-Gel: Size-Dependent Properties, Surface Modification, and Applications in Silica-Polymer Nanocomposites—A Review. J. Nanomater. 2012, 132424.

35. Singh, L.; Bhattacharyya, S.; Kumar, R.; Mishra, G.; Sharma, U.; Singh, G.; Ahalawat, S. Sol-Gel processing of silica nanoparticles and their applications. Advances in Colloid and Interface Science. 2014. https://doi.org/10.1016/j.cis.2014.10.007

36. Kumar, S.; Malik, M. M.; Purohit, R. Synthesis Methods of Mesoporous Silica Materials. Mater. Proc. 2017, 4, 2A, 350–357.

37. Costa, J. A. S.; Jesus, R. A. de; Santos, D. O.; Neris, J. B.; Figueiredo, R. T.; Paranhos, C. M. Synthesis, functionalization, and environmental application of silica-based mesoporous materials of the M41S and SBA-n families: A review. J. Environ. Chem. Eng. 2021, 9, 105259.

38. Emrie, D. B. Sol–Gel Synthesis of Nanostructured Mesoporous Silica Powder and Thin Films. J. Nanomater. 2024.

39. Ling, F. W. M.; Abdulbari, H. A.; Sim-Yee, C. Synthesis and characteristics of silica nano-particles using modified sol–gel method in microreactor. Mater. Proc. 2021, 42, 1, 1–7.

40. Lofgren, J. E.; Ozin, G. A. Controlling morphology and porosity to improve performance of molecularly imprinted sol–gel silica. Chem. Soc. Rev. 2014, 43, 572–588.

41. Sharafi, Z.; Backshi, B.; Javidi, J.; Adrangi, S. Synthesis of Silica-coated Iron Oxide Nanoparticles: Preventing Aggregation without Using Additives or Seed Pretreatment. IJPR. 2018, 17, 1, 386-395.

42. Fusinato, M.; Farias da Silva Amaral, M.; Irigon de Irigon, P.; Calgaro, C.; Gil de Los Santos, D.; Filho, P. Silica extraction from rice hull ash through the sol-gel process under ultrasound. Environ Sci Pollut Res Int. 2022. https://doi.org/10.1007/s11356-022-23687-1

43. K. P. Priyanka, N. Aloysius Sabu, A. T. Sunny, P. A. Sheena, and T. Varghese, “Effect of Electron Beam Irradiation on Optical Properties of Manganese Tungstate Nanoparticles,” *Journal of Nanotechnology*, vol. 2013, Article ID 580308, 2013. DOI: 10.1155/2013/580308.

44. Mourhly, A.; Khachani, M.; El Hamidi, A.; Kacimi, M.; Halim, M.; Arsalane, S. The Synthesis and Characterization of Low-Cost Mesoporous Silica SiO2 from Local Pumice Rock. Nanomaterials 2015, 5, 1-7.

45. Ayral, A. Sol-Gel Synthesis and Fine Characterization of Hierarchically Porous and Multifunctional Silica-Based Membranes. Catalysis Today 2018, 204, 121-128.

46. Ismail, A.; Saputri, L. N. M. Z.; Dwiatmoko, A. A.; Susanto, B. H.; Nasikin, M. A facile approach to synthesis of silica nanoparticles from silica sand and their application as superhydrophobic material. J. Asian Ceram. Soc. 2021, 9, 665–672.

47. Bokov, D.; Jalil, A. T.; Chupradit, S.; Suksatan, W.; Ansari, M. J.; Shewael, I. H.; Valiev, G. H.; Kianfar, E. Nanomaterial by Sol-Gel Method: Synthesis and Application. Journal of Nanomaterials. 2021, 5102014.

48. Fuertes, A. B.; Valle-Vigón, P.; Sevilla, M. Synthesis of colloidal silica nanoparticles of a tunable mesopore size and their application to the adsorption of biomolecules. J. Colloid Interface Sci. 2010, 349, 173–180.

49. Vivar Mora, L.; Taylor, A.; Paul, S.; Dawson, R.; Wang, C.; Taleb, W.; Owen, J.; Neville, A.; Barker, R. Impact of silica nanoparticles on the morphology and mechanical properties of sol-gel derived coatings. Surf. Coat. Technol. 2018, 342, 48–56.

50. Hessien, M.; Prouzet, E. Synthesis of Hierarchical Porous Silica by Sol-Gel of Sodium Silicate and Nanoemulsion Templating: Effective Combination Conditions. Chem. Sel. 2021, 6, 1440-1447.

51. Borlaf, M.; Moreno, R. Colloidal sol-gel: A powerful low-temperature aqueous synthesis route of nanosized powders and suspensions. Open Ceram. 2021, 8, 100200.

52. Vazquez, N.I.; Gonzalez, Z.; Ferrari, B.; Castro, Y. Synthesis of mesoporous silica nanoparticles by sol-gel as nanocontainer for future drug delivery applications. Bol. Soc. Esp. Cerám. Vidr. 2017, 56, 139-145.

53. Liberman, A.; Mendez, N.; Trogler, W.C.; Kummel, A.C. Synthesis and surface functionalization of silica nanoparticles for nanomedicine. Surf. Sci. Rep. 2014, 69, 132-158.

54. Vallet-Regi, M.; Tamanoi, F. Overview of Studies Regarding Mesoporous Silica Nanomaterials and Their Biomedical Application. The Enzymes 2018, 43, 1-10.

55. Pan, L.; Wang, Y.; Xu, H.; Ding, Y.; Li, Y.; Zhao, J. Synthesis of Silica Particles with Precisely Tailored Diameter. Chin. J. Chem. 2014, 27, 563-567.

56. Suriyaprabha, R.; Karunakaran, G.; Kavitha, K.; Yuvakkumar, R.; Rajendran, V.; Kannan, N. Application of silica nanoparticles in maize to enhance fungal resistance. IET Nanobiotechnol 2014, 8, 133-137.

57. Jeelani, P.G.; Mulay, P.; Venkat, R.; Ramalingam, C. Multifaceted Application of Silica Nanoparticles. A Review. Silicon. 2019, 12, 1337-1354.

58. Peng, R.; Khan, M.A.; Liu, C.L. Synthesis of Silica nanoparticles and their application of Dielectric relaxation spectroscopy- a review. Results Chem. 2023, 6, 101218.

59. Yamamoto, E.; Kuroda, K. Colloidal Mesoporous Silica Nanoparticles. Bull. Chem. Soc. Jpn. 2016, 89, 501-539.

60. Zhang, W.; Liu, H.; Qiu, X.; Zuo, F.; Wang, B. Mesoporous silica nanoparticles as a drug delivery mechanism. Open Life Sci. 2024, 19(1), 20220867.

61. Manoj, S.; Cheng, D.; Qu, J.; Song, H.; Yu, C.; Ganguli, A.; Tang, J. ZIF-90-Decorated Silica Nanoparticles with a Spiky Surface: A Novel Approach for Drug Delivery. New Journal of Chemistry. 2024, 48, 5760-5768.

62. Yang, Y.; Zhan, W.; Role of Tissue Hydraulic Permeability in Convection-Enhanced Delivery of Nanoparticle-Encapsulated Chemotherapy Drugs to Brain Tumour. Pharm. Res. 2022, 39, 877–892.

63. Vivero-Escoto, J.L.; Slowing, I.I.; Wu, C.; Lin, V.S. Photoinduced Intracellular Controlled Release Drug Delivery in Human Cells by Gold-Capped Mesoporous Silica Nanosphere. J. AM. CHEM. SOC. 2009, 131, 3462-3463.

64. Tielmann, P.; Kierkels, H.; Zonta, A.; Illie, A.; Reetz, M.T.; Increasing the activity and enantioselectivity of lipases by sol-gel immobilization: further advancements of practical interest. Nanoscale. 2021, 6(12), 6220-8.

65. Suriyaprabha, R.; Karunakaran, G.; Yuvakkumar, R.; Rajendran, V.; Kannan, N. Foliar Application of Silica Nanoparticles on the Phytochemical Responses of MAize (Zea mays L.) and Its Toxicological Behavior. Synth. React. Inorg. Met.-Org. Nano-Met. Chem. 2014, 44, 1128-1131.

66. Akhayere, E.; Kavaz, D.; Vaseashta, A. Synthesizing Nano Silica Nanoparticles from Barley Grain Waste: Effect of Temperature on Mechanical Properties. Pol. J. Environ. Stud. 2019, 28, 2513-2521.

67. Patel, M.; Mishra, S.; Verma, R.; Shikha, D. Synthesis of ZnO and CuO nanoparticles via Sol gel method and its characterization by using various techniques. Discov. Mater. 2022, 2, 1.

68. Chen, Y.; Zhan, J.; Zhang, P.; Nie, S.; Lu, H.; Song, L.; Hu, Y. Preparation of Intumescent Flame Retardant Poly(butylene succinate) Using Fumed Silica as Synergistic Agent. Ind. Eng. Chem. Res. 2010, 49, 8200-8208.

69. Ghamarpoor, R.; Jamshidi, M. Synthesis of vinyl-based silica nanoparticles by sol-gel method and their influences on network microstructure and dynamic mechanical properties of nitrile rubber nanocomposites. Sci. Rep. 2022, 12, 15286.

70. Zhan, W.; Chen, L.; Kong, Q.; Li, L.; Chen, M.; Jiang, J.; Li, W.; Shi, F.; Xu, Z. The Synthesis and Polymer-Reinforced Mechanical Properties of SiO2 Aerogels: A Review. Molecules 2023, 28, 5534.

71. Zadeh, M. M.; Amiri, F.; Hosseini, S.; Arabloo, M. Synthesis of Colloidal Silica Nanofluid and Assessment of its Impact on Interfacial Tension and Wettability for Enhanced Oil Recovery. SSRN 2023.

72. Vashistha, P.; Singh, S. K.; Dutt, D.; Kumar, V. Sustainable utilization of paper mill solid wastes via synthesis of nano silica for production of belite based clinker. J. Cleaner Prod. 2019, 224, 557–565.

73. Zulfiqar, U.; Subhani, T.; Husain, S. W. Synthesis of silica nanoparticles from sodium silicate under alkaline conditions. J. Sol-Gel Sci. Technol. 2016, 77, 753–758.

74. Liu, Q. X.; Xu, W. C. Application of Precipitated Silica in Print Coated Paper Coating. In Advanced Materials Research, 2012, 468-471, 2183-2186.

75. Parashar, M.; Shukla, V. K.; Singh, R. Metal oxides nanoparticles via sol–gel method: a review on synthesis, characterization and applications. J. Mater. Sci.: Mater. Electron. 2020, 31, 3729–3749.

76. Deshmukh, K.; Kovářík, T.; Křenek, T.; Docheva, D.; Stich, T. Pola, Recent advances and future perspectives of sol–gel derived porous bioactive glasses: a review. J. RSC Adv. 2020, 10, 32474–32488.

77. Barhoum, A.; Van Assche, G.; Rahier, H.; Fleisch, M.; Bals, S.; Delplancke, M.-P.; Leroux, F.; Bahnemann, D. Sol-gel hot injection synthesis of ZnO nanoparticles into a porous silica matrix and reaction mechanism. Materials & Design. 2017, 119, 270-276.

78. Gosiamemang, T.; Heng, J. Sodium hydroxide catalysed silica sol-gel synthesis: Physicochemical properties of silica nanoparticles and their post-grafting using C8 and C18 alkyl-organosilanes. Powder Technology. 2023, 417, 118237.

79. Jafarzadeh, M.; Rahman, I.A; Sipaut, C.S. Synthesis of silica nanoparticles by modified sol–gel process: the effect of mixing modes of the reactants and drying techniques. J Sol-Gel Sci Technol. 2009, 50, 328–336.

80. Capeletti, L. B.; Cardoso, M.B.; Dos Santos, J. H. Z.; He, W. Hybrid Thin Film Organosilica Sol-Gel Coatings To Support Neuronal Growth and Limit Astrocyte Growth. ACS applied materials & interfaces. 2016, 8, 41, 27553–27563.

81. Abburi, A.; Ali, M.; Velagaleti, M.P. Synthesis of mesoporous silica nanoparticles from waste hexafluorosilicic acid of fertilizer industry. JMR&T. 2020, 9, 41, 8074-8080.

82. Knossalla, J.; Mezzavilla, S.; Schüth, F. Continuous synthesis of nanostructured silica based materials in a gas–liquid segmented flow tubular reactor. New J. Chem. 2016, 40, 4361-4366.

83. Barker, C.R.; Lewns, F.K.; Poologasundarampillai, G.; Ward, A.D. In Situ Sol–Gel Synthesis of Unique Silica Structures Using Airborne Assembly: Implications for In-Air Reactive Manufacturing. ACS Appl. Nano Mater. 2022, 5, 8, 10373–10384.

84. Ronda, L.; Bruno, S.; Campanini, B.; Mozzarelli, A.; Abbruzzetti, S.; Viappiani C.; Cupane, A.; Levantino, M.; Bettati, S. Immobilization of Proteins in Silica Gel: Biochemical and Biophysical Properties. Curr. Org. Chem. 2015, 19, 1653–1668.

85. Ling, F. W. M.; Abdulbari, H. A.; Sim-Yee, C. Effect of residence time on the morphology of silica nanoparticles synthesized in a microfluidic reactor. J. Flow Chem. 2021.

86. Yu, J.; Dan, N.; Eslami, S.M.; Lu, X. State of the art of silica nanoparticles: An overview on biodistribution and preclinical toxicity studies. AAPS J. 2024, 26, 35.

87. Zhang, Y.; Lin, X.; Chen, X,; Fang, W.; Yu, K.; Gu, W.; Wei, Y.; Zheng, H.; Piao, J.; Li, F. Strategies to regulate the degradation and clearance of mesoporous silica nanoparticles: A review. Int. J. Nanomedicine 2024, 5859–5878.