

A Review on Synthesis, Characterization and Applications of Silica Particles

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ABSTRACT

The developments of polymeric, liposomal and inorganic nanoparticles find scope for diagnostic and therapeutic applications. Silica particles are of promising material in biomedical, photovoltaic and energy storage due to their size dependent optoelectronic properties. Silica nanoparticles can be produced using synthetic techniques with a precise size control and physical and chemical properties. The recent advancement in the development of the silica particle of different sizes due to its enhanced biocompatibility are applied in pharmaceutical, drug delivery and in the waste water treatment applications are highlighted. In this review the synthesis, analysis, properties, characterization methods and applications of silica nano particles in biomedical imaging, drug delivery vehicles, diagnostic and therapeutic field are highlighted.

Keywords – *Dynamic Light scattering; Nanoparticle; scanning Electron Microscopy; Silica; Ultrasonic; Spherical; Stober's process.*

I. INTRODUCTION

Silica particles are considered to be a promising candidate for drug delivery due to its favorable chemical properties, thermal stability, and biocompatibility. The properties including pore size, high drug loading, and porosity as well as the surface properties, are used widely in the field of diagnosis, target drug delivery, bio-sensing, cellular uptake. The following sections present the various methods, characterization and applications of silica particles.

The silica particles are first synthesized by Stober's in the year 1968, using tetraethyl ortho silicate (TEOS) or other silicates, alcohol, and ammonia with a desired size. The Stöber method can be employed without templates to form solid particles.

Werner Stober et al., 1968 developed monodisperse silica spheres ranging from 50 nm to 2000 nm by the hydrolysis of alkyl silicates followed by condensation of silicic acid in alcoholic solutions using ammonia catalyst. The characterization and size of the synthesized

particles were performed using Scanning Electron microscopy (SEM) and dynamic light scattering method (DLS).

Kota Sreenivasa Rao et al., 2005 developed a novel method for the synthesis of silica nanoparticles by sol-gel method accompanied by ultra-sonication. The effect of concentration of the reagents with particle size was studied. The study showed that the particle size decreased with increase in reagent concentration. The surface characterizations of the synthesized particles are analyzed using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). The results obtained in the research are in agreement with the results observed for the electronic absorption behavior of silica nanoparticles, measured using UV-vis spectroscopy.

The study by Xiao Dong Wang et al., 2003 shoes the preparation of silica particles of size ranges from 20 nm to 1000 nm by stober's process using high concentrations of Tetra Ethyl Ortho Silicate (TEOS). The influences of TEOS, NH₃ and H₂O are studied with respect to particle size and size distribution. Finally a modified monomer addition model combined with aggregation model is proposed to analyze the formation mechanism of silica particles.

A research by Nicolas Plumere et al., 2010 discussed about the preparation of special purpose silica particles in the size range 50 nm - 800 nm with desired particle shape, size, poly dispersity, and porosity and free from aggregation. Characterization of these particles was done using Scanning Electron Microscopy (SEM), Dynamic Light Scattering (DLS), nitrogen sorption isotherms, Gay-Lussac pycnometry and DRIFT spectroscopy. The particle diameter was maintained by managing the reaction temperature and ammonia concentration. The particles were monodisperse in nature due to the fact that the reaction temperature was homogenized and at high temperatures particles of sizes less than 100 nm were produced.

A novel method for the synthesis of monodisperse gold-coated silica nanoparticles was performed by Michael D. English and Eric R. Waclawik, 2012 using Stober's

protocol. The study focused on the development of silica particles of size ranges from 45 nm to 460 nm. Silica hydroxyl groups were deprotonated in the presence of ACN thereby generating a formal negative charge on the siloxy groups. The particle size that ranged from 400 nm to 480 nm was used for gold-coating experiments. Characterization of these particles was done using SEM, TEM and EDX (Energy Dispersive X-ray spectroscopy). Electron diffraction results indicated that the gold shell was poly-crystalline and non-directional in orientation. UV-Vis spectroscopy results showed a reduction in intensity with an increase in the incident irradiation wavelength.

Adrian Ruff, et al., 2013 studied the preparation of silica particles with a size of 125 nm and its characterization using spectroscopic and electrochemical methods. The two main parameters manipulated are the temperature and post calcinations steps. High temperatures and a post synthetic calcination step lead to the yielding of nonporous, low polydisperse silica spheres, whose diameter is approximately 125 nm. Fourier transform infrared spectroscopy (FTIR), UV-Vis and Energy Dispersive X-ray Spectroscopy was applied for the characterization of particles. These Viologen modified particles are treated with $\text{Na}_2\text{S}_2\text{O}_4$ which leads to the formation of Nano particulate silica material having stable free radicals located at the particle surface, and this formation was verified using EPR and UV/Vis Spectroscopy.

Fei Wang, Ziheng Li et al., 2010 developed the magnetic mesoporous silica composites by incorporating Magnetic Fe_3O_4 using modified stobers protocol. Nano- Fe_3O_4 particles were dispersed into the water in ethanol micro emulsion using Cetyl trimethyl ammonium bromide as a surfactant. The particles that were produced ranged between 120 nm - 380 nm in size and showed signs of being above average drug delivery platforms for photodynamic therapy. These nanoparticles also showed good magnetic responsiveness and biological adaptation performance.

Highly concentrated monodisperse silica particles were synthesized by Kiyoharu Tadanaga, et al., 2013 using stober's protocol. Tetraethoxy silane is used as the primary reactant. 4% by weight of silica nanoparticles having diameter of about 10 nm were obtained by manipulating the reaction conditions. When the solvent was removed under reduced pressure, the particle concentration went up to 15% by weight without aggregation.

Canton, et al., 2011 developed dye-doped silica nanoparticles with high photo stability and ultra-sensitivity for the application of bio sensing and bio imaging. The synthesis methodology used are Stober synthesis and micro emulsion of which stober's method gave better result. Particles that are within the sizes of 10-50 nm hold greater promise in this field than the particles that are of larger sizes. One modification in the Stober's protocol done was that the entire reaction takes place in the presence of Amino propyl triethoxy silane (APTEOS) linked to Alexa Fluor 555 in order to get dye doped nano particles that have high photo stability and long fluorescence lifetime as compared to free dyes.

Amino functionalized silica nanoparticles of size around 40 nm are synthesized by Hsu-Tung Lu, et al., 2013. The reagents used for the preparation of nanoparticles are TEOS, methanol and Ammonia and the resulting nanoparticles were functionalized using 3-aminopropyltrimethoxysilane. The characterization of the raw and amino functionalized samples is carried out using FTIR and SEM. The adsorption-desorption isotherms of the amino-functionalized silica nanoparticles were found to be nonporous.

David Lawrence Green, year had studied the dynamics of nanophase formation of silica particles and the nucleation and aggregation dynamics of the prepared particles are studied using nuclear magnetic resonance, small-angle X-ray scattering, Dynamic light Scattering, Doppler electrophoretic light scattering and transmission electron microscopy. The study showed that the nanoparticles formed using methanol as one of the reagents was more stable than those produced using ethanol as the reagent in place of methanol. Also aggregation of nanoparticles occurred during the addition of salt.

Singh, V. K., et al., 2014 synthesized silica and graphene oxide nanoparticles using stober's protocol and the mechanical properties of the Silica/Graphene oxide composite powders were characterized by FTIR spectroscopy, X-ray diffraction analysis, TEM and SEM. The use of graphene oxide as a reinforcement helps improve the mechanical properties of silica along with its electrical conductivity and adsorption properties.

Leen C.J., Thomassen, et al., 2009 prepared silica particle sols for *in vitro* cytotoxicity testing. The size of the nanoparticles ranged from 2 nm to 335 nm and this was determined using Dynamic Light Scattering (DLS). The particle morphology, surface area and porosity were characterized using Scanning Electron Microscopy

(SEM) and nitrogen adsorption. The relationship between cytotoxicity and particle size were studied using human endothelial and mouse monocyte-macrophage cells. The results showed a strong link between silica particles' cytotoxicity and its size and cell type.

Diego Adolfo Santamaria Razo, et al., 2008 prepared mono-disperse silica Nano spheres of size around 400 nm for the fabrication of opal photonic crystals in a single step process by controlling the TEOS concentration and maintaining a uniform concentration of ammonia, water and ethanol, it was possible to manipulate the particle diameter (particle diameter > 400 nm) and mono dispersity of silica nano particles.

Alexander Liberman, et al., 2014 synthesized silica nanoparticle of size between 10 nm -1500 nm and functionalized the same particle for various applications in nano medicine. TEM, SEM and FTIR are employed for the characterization of the raw and functionalized particles.

J. H. Zhang, et al., 2003 studied the influence of change in reagent concentrations with respect to size, shape and mono dispersity of the silica particles. Continuous addition of Tetra Ethyl Ortho Silicate increased the size of silica particles, which varied from 150 nm to 1.2 μm . Scanning Electron Microscopy (SEM) and Transmission Emission Microscopy (TEM), were used to characterize the prepared particles.

Ismail A.M., Ibrahim, et al., 2010 developed spherical silica nanoparticles and discussed the effect of Tetra Ethyl Ortho Silicate (TEOS) and ammonia concentrations in the diameter of silica particles during the nucleation and growth processes. Hexa methyl di silane was used as a surface modifier to prevent the particle aggregation and hence to increase the dispersion. Transmission Emission Microscopy (TEM) was used for characterization of the particles.

Nozawa, et al., 2005 discussed the smart control of monodisperse stober silica particles and the effect of reactant addition rate on growth process. The desired particle size was 1 μm to 2 μm . The method devised is also a cost effective one. Characterization is done using Scanning Electron Microscopy (SEM), Dynamic Light scattering (DLS) and particle size analyzer.

Marie Ivarsson, et al., 2013 focused on the synthesis of silica particles by modified stober's method for the use as probe in diffusion by Fluorescence Recovery after Photo bleaching FRAP and Nuclear Magnetic Resonance Diffusometry NMR-diffusometry Probes for

measuring diffusion. FITC (Fluorescein isothiocyanate) was used to make the particles fluorescent and visible to FRAP. Stokes-Einstein equation is used to calculate the average particle sizes with the sizes from the diffusion rates. It was found out from studies that lower alcohols and a lower alkyl silicate, for example methanol and tetramethyl ester respectively, help narrow down the size distribution. Ammonia, which acts a catalyst in Stober process, also is the reason behind the spherical shape of the silica particles. It also helps reduce flocculation. The particles produced had a size above 100 nm.

Roberto Sato-Berru, et al., 2013 developed simple method for the controlled growth of silica spheres ranging from 10 nm to 600 nm. The synthesis of particles was carried out by changing the ethanol/ water ratio in a reactive system. The characterization of silica particles was done using Transmission Emission Microscopy (TEM) and Dynamic Light scattering (DLS).

Ismail Abdul Rahman and Vejayakumaran Padavettan, 2012 reviewed the synthesis of silica Nanoparticles by Sol-Gel method and its Size-Dependent Properties, Surface modification and applications in Silica-Polymer Nano composites are compared with other methods. The application of particles thus formed is used as fillers in silica-polymer nano composites, biotechnology and drug delivery among many others. The surface characterizations of the particles are done using Scanning Electron Microscopy (SEM).

Gorji, et al., 2012 studied the synthesis and characterizations of silica nanoparticles by a new Sol-Gel Method. The silica nanoparticles were synthesized using TEOS, polyethylene glycol and hydrochloric acid (0.001 N). The synthesis led to the formation of high purity silica particles of size of approximately 34 nm. Characterization methods applied were Scanning Electron Microscopy (SEM), Transmission Emission Microscopy (TEM) and X-ray Diffraction.

Tabatabaei et al., 2006 studied the synthesis of silica particles of narrow size distribution by chemical method using tetra ethyl ortho silicate (TEOS), ethanol and deionized water in the presence of ammonia as catalyst at room temperature. The morphology and the average diameter of colloidal silica particles depend on the proportion of the reactants. Silica nanoparticles were obtained via the same molar ratio of TEOS, ammonia and also a high molar ratio of ethanol. The nature and morphology of the synthesized particles was investigated by scanning electron microscopy (SEM), transmission

electron microscopy (TEM), transmission electron microscopy (TEM) and X-ray diffraction (XRD).

Usama Zulfqar, et al., 2016 developed silica particles using Bentonite clay by acid and thermal treatment method. Three different size ranges of silica nanoparticles are produced at low concentrations of clay. A range of silica particle sizes from nanometer to micrometer was obtained by varying the contents of silica rich clay, HNO_3 , and ethanol. It was observed that the concentration of silica rich clay and HNO_3 had a direct effect on the particle size. The increase in the quantity of ethanol from 10 ml to 20 ml produced bimodal particles of nanometer and micrometer size, which maintained at 30 ml. inductively coupled plasma, optical emission spectroscopy, atomic absorption spectroscopy, X-ray fluorescence, scanning electron microscopy and X-ray diffraction were utilized to characterize the clay, SSS and nanoparticles.

Delyan R. Hristov et al., 2015 described the control of size homogeneity in silica nanoparticles, prepared by a two phase arginine catalyzed aqueous method, through varying the upper organic solvent phase. The final particle dispersion characteristics can be controlled by varying features including solvent type and interfacial area, related to the rate of monomer transfer at the TEOS/water interface.

Stanley and Samson Nesara, 2014 performed the wet chemical synthesis of SiO_2 nano particles using tetraethyl orthosilicate (TEOS), ethanol, water and ammonium hydroxide with surfactants (CTAB, PVP and SDS) is reported. The characterizations of particles are carried out using SEM EDX, TEM, XRD, FTIR and UV- Visible spectroscopy. The XRD data obtained on SiO_2 powder shows that all samples are amorphous in nature. The EDAX data confirmed the presence of silicon and oxygen in all the samples. From the FTIR data, it was shown that all samples exhibited characteristic peaks for SiO_2 . The particulate properties obtained on SiO_2 powder suggest that the particles are present from nano to micrometer size. SEM data revealed that SiO_2 samples prepared with the addition of 2 % or 3 % SDS (surfactant) resulted in less particle size than other samples.

Banafsheh Gorji, et al., 2012 developed a simple method for the preparation of nano porous silica based on the sol-gel process. Amorphous silica nanoparticles with regular spherical structure were obtained successfully using TEOS as a precursor. The inner diameter of Nano pore size is about 34 nm. It was found

the following synthesis parameter must be taken into consideration in synthesis of silica nanoparticles using TEOS. In order to achieve the best conditions for performing silica nanoparticles, the optimal parameters should be considered. This will enhance the use of silica in many applications in many fields such as catalysis.

Singh, 2011 studied the synthesis of spherical and amorphous silica nanoparticles by the hydrolysis of TEOS in ethanol using water and ammonia using sol-gel method. The particle size of nano silica can be controlled by adding span 20, span 40 and span 60 surfactants. The size of nano silica powder also depends on the pH value of reaction system. Particle size increases with the increase of the pH of the reaction system. It was observed from SEM, XRD and TGA studies that addition of n- SiO_2 to cement reduced CH leaching by reacting at early stage of hydration and forming additional C-S-H gel. It was found that, CH content in n- SiO_2 incorporated cement paste reduced approximately ~89% at 1 day and up to approx. 60% at 28 days. Therefore, addition of small quantity of n- SiO_2 significantly improves the morphology and mineralogy of the cementitious materials.

SiO_2 nanoparticles were successfully synthesized by M. A. Dabbaghian, et al., 2010 via sol-gel precipitation method and the effects of different parameters such as temperature, ethanol, ammonia and tetra ethyl ortho silicate (TEOS). It was found that, among all the investigated parameters, ethanol as a co-solvent, had the greatest significant effect on the size of the synthesized silica nanoparticles, so that increasing the amount of ethanol led to initially bigger and then smaller particle size. Temperature had an inverse effect on the particle size, i.e. particle size decreased by increasing the temperature. In addition, the remaining variables, TEOS and ammonia, showed similar trends to that of ethanol in two opposing ways. This novel exploration of size distribution (SD) indicated that particle size was proportional to the SD, so that the narrowest SD was attained at the lowest particle size and vice versa.

Spherical silica nanoparticles with various sizes have been synthesized by micelles entrapment approaches were studied by Nor Ain Zainal, et al., 2013. The study investigated the effect of synthesis parameters (stirring speed, pH and amount of surfactant) on particle size of silica nanoparticles. It was found that the average size of silica particles depend on the proportion of the reactants and temperature. By adjusting the reaction temperature, the silica nanoparticles with average size of 28.91 nm – 113.22 nm were obtained. 2-butanol as a solvent in the

preparation method also has much influence on the size of silica nanoparticles. As a result, varying their parameters during the synthesis process give the different sizes of silica nanoparticles entrapped rifampicin. The amount of the alcohol and silica precursor, and also temperature were proportional to the nanoparticle size as a response.

Murray, E., et al., 2010 compared the various routes of silica particle synthesis. Monodisperse colloidal silica particles with diameters of 15nm - 25 nm were prepared via the hydrolysis of tetraethyl orthosilicate (TEOS) by aqueous ammonia in ethanol. The surfaces of these particles were rendered hydrophobic with octadecyltrimethoxysilane (ODTMS) after the reaction or, more conveniently, during the growth phase. Secondly, silica particles with diameters of 15 nm - 50 nm were prepared using a one-pot synthesis in which TEOS was hydrolyzed by an amino acid and the resulting particles were coated with ODTMS. Lastly a novel, direct approach to the synthesis of hydrophobic organo silica nanoparticles was developed using ODTMS as the single silica source. Hydrolysis of the ODTMS by aqueous ammonia in ethanol yielded monodisperse colloidal organo silica particles with diameters of 15 nm - 30 nm.

Mohammad Senemar, et al., 2016 developed a facile and novel method for synthesis of amorphous silica nanoparticles by pyrolysis and combustion of HTV silicone at 700 °C for 1 h, including heating up time from ambient temperature at heating rate of 20°C/min. The synthesized particles were characterized by XRD, DLS, FTIR, BET, FESEM and TEM. XRD analysis revealed a diffuse peak at 2θ of 22° matching that of amorphous silica. FTIR investigation of the particles showed the Si–O–Si bond. BET and DLS tests confirmed surface area and the average particle size in the range of 10-50 nm, while FESEM and TEM analyses showed surface morphology.

Mani Ganesh and Seung Gil Lee, 2013 studied the synthesis of meso porous silica nanoparticle (MSNs) with high surface area and pore volume using Triton X-100 as main and Tween 60 as co-template (at various concentrations). Ibuprofen a water insoluble model drug was loaded into the synthesized silica nano particle and studied for sustained release capability. Characterization techniques used are FTIR, Diffuse reflectance UV spectroscopy (UV-DRS), Brunauer Emmett Teller (BET) technique, Differential Scanning Calorimetry (DSC), Thermo gravimetric analysis (TGA), powder XRD and scanning electron microscopy (SEM) for the

morphology and drug loading. From the results it was noted that the entire silica nanoparticle synthesized by sol-gel was mesoporous with high surface area and pore volume.

Laleh Maleknia, et al., 2013 developed an easy and economic method for the synthesis of silica powder using low cost materials such as sodium silicate and reduce synthesis time to a maximum of 4 hrs. According to this method was more affordable than the previous synthesis methods sodium silicate and HMDS and nitric acid were mixed for the organic modification of hydrogels in the aqueous phase. Surface morphology of the particles was investigated using SEM revealed that the average size of the Nano-particles is 16 nm. FTIR test also approved the existence of Methyl groups at hydrophobic Nano silica structure.

Mesoporous nano silica particles of size around 20 nm were prepared by Yi, Zhifeng, Feng, et al., 2015. The reaction conditions were maintained at low temperature and the pH value of the reaction solution was found to have a great impact on the morphology of the final products. The surface characterization of the particles was investigated through transmission electron microscope and surface area was examined by Brunauer-Emmett-Teller and Barrett-Joyner-Halenda methods. The results suggested that the high pH value had a great effect on the morphology of the final MSNs. Higher pH value intensified the interaction between particles.

Functionalized silica core particles were prepared by hydrolysis and condensation of tetra ethyl ortho silicate Milan Nikolić, et al., 2010. Core-shell particles were formed by deposition of primary particles synthesized from sodium silicate solution on functionalized silica core particles prepared by hydrolysis and condensation of tetra ethyl ortho silicate. Average shell thickness is about 60 nm that is consisted of primary silica particles with average size of ~21 nm. Zeta potential measurements and SEM analysis showed that continuous shell exists around core particles. FTIR measurements indicated on the complex structure of core-shell particles and meso porous structure of shell was confirmed by TEM measurement.

Qu, et al., 2013 investigated the importance of innovative technologies in integrated water management. The study focused on the application of different types of nanomaterials in water treatment and its properties and mechanisms of application.

Le, et al., 2014 recommends SiO₂ as one of the most versatile nanoparticles, for wide range of applications such as wastewater treatment, environmental remediation, food processing, manufacturing of insecticides etc. The study shows that silica nanoparticles have affected the contents of Cu, Mg and Na in the roots and shoots of transgenic cotton. Silica nanoparticles also influenced the SOD activity and IAA concentration.

II. CONCLUSION

Silica is a widespread inorganic nanomaterial having extensive range of applications including fillers for rubber, bio catalysis supports, selective adsorption and removal of pollutants from air, carriers in food and agriculture, and abrasive/anticaking agents in cosmetics. It is also widely believed to be an important material for biomedical and drug delivery applications. This review provides an outline of different types of synthesis methods, chemistry, and applications of silica, followed by an overview of the characterization techniques employed.

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