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REVIEW

A Review on the Heightened Mechanical Features of Nanosilica-Based Concrete and the Response of Human Fibroblasts to Nanosilica

Eribe M. Jonathan[1] · Ikhazuagbe H. Ifijen[2] · Kate E. Mokobia[3] · Emmanuel I. Okeke[4] · Chiadika I. Omoruyi[4] · Bala Anegbe[5]

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Abstract
Cement is utilized extensively in the manufacturing of concrete, which makes it the most common material used in building construction. However, the usage of a great deal of cement results in a great deal of CO_2 emissions, which leads to the greenhouse effect. Numerous studies have developed the use of nano-SiO_2 in concrete materials to lower the cement content of concrete mixtures while improving mechanical properties. Additionally, a number of studies have demonstrated that silica NPs trigger an inflammatory response in pulmonary fibroblasts. The main cells that produce and maintain the extracellular matrix (ECM) in the connection of the tissue are fibroblasts. Fibroblasts are involved in processes including tissue regeneration and wound healing. Similar to angiogenesis, inflammation, cancer, and pathological and physiological tissue fibrosis, fibroblasts act as intermediaries. The effect of silica nanoparticles on the mechanical properties of concrete (compressive strength, split tensile strength, and flexural strength) was succinctly presented in this paper. Likewise, a number of studies on the reaction of human fibroblasts to silica nanoparticles were evaluated. Numerous research on the addition of silica nanoparticles to concrete revealed that doing so significantly enhanced the material's mechanical properties. The controlled interaction of silica nanoparticles with human fibroblast cells was demonstrated to have potential in a number of applications, including aesthetics, intracellular drug release systems, improving scar tissue, determining the fate of biomaterials in vivo, and designing potential prosthetics and implant surfaces to reduce bacterial adhesion.

Keywords Concrete · Human fibroblasts · Cells · Nano-silica · Mechanical features

Introduction

Modernization and industrial enterprise pose a serious threat to the environment, which has led to air pollution. For 5–8% of the CO_2 released globally, which contributes to global warming, the carbon dioxide (CO_2) emission from the manufacturing of cement [1] is responsible. To reduce the impact of CO_2 emissions caused by cement manufacturing activities in concrete, several compounds have been identified and used to substitute cement [2]. These materials exhibit pozzolanic properties. The outstanding qualities of nano- or microstructured materials, such as their increased surface area to volume ratio, aspect ratio, and better optical characteristics, have been demonstrated [3–15]. To minimize environmental pollution, materials with these characteristics have been utilized to partially replace cement in the manufacturing of concrete, including micro- or nano-silica and silica fume [2]. Numerous studies have examined and supported the usage of nano-silica as a cement replacement [1, 16].

By reacting with lime (CH) during cement hydration and inducing the development of hydrated calcium silicates (C–S–H) phase, nanosilica (nano-SiO_2) improves the durability and mechanical strength of concrete [17]. The use of nanosilica can significantly increase strength, compaction,

✉ Ikhazuagbe H. Ifijen
larylans4u@yahoo.com

1 Department of Chemistry, Benson Idahosa University Benin City, PMB 1100, Edo State, Nigeria

2 Department of Research Operations, Rubber Research Institute of Nigeria, Iyanomo, Benin City, Nigeria

3 Department of Science Laboratory Technology, Delta State Polytechnic, Otefe-Oghara, Delta State, Nigeria

4 Department of Chemistry, University of Benin, Benin City, Edo State, Nigeria

5 Department of Industrial Chemistry, Faculty of Science, Federal University, Oye-Ekiti, Nigeria

and hydration of the microstructure of cement matrix [18, 19]. The proper dispersion of nanosilica in cement-based materials can expedite the hydration of the cement paste and the microstructure of the paste [19]. Physical or chemical methods can be used to create nanosilica [20, 21]. However, it is still exceedingly difficult to get a sufficient nanosilica dispersion in the cement matrix. Due to their high surface energy, too many nanoparticles may aggregate, decrease mechanical performance, and locally increase porosity [22, 23]. As an industrial product, nanosilica is often used as a water suspension having particles with diameters between 40 and 140 nm and an average concentration of 10 to 50% of nano-SiO_2 [19]. An earlier study found that nanoparticles can slow down the deterioration of cement-based composites brought on by high temperatures [24, 25]. This capacity makes a significant contribution to ensuring adequate concrete fire resistance. By improving the particle packing in the cement matrix and filling the micropores with nanosilica, it is possible to significantly reduce spalling during a fire [26, 27]. In the past, different nanomaterials have been chemically modified using the "protective" properties of nanosilica at high temperatures.

In the area of biomedicine, silica nanoparticle research has made promising progress (NPs). NPs can be used for DNA delivery, phototherapy, controlled medication delivery, bioimaging, and other medical procedures [28–31]. Furthermore, depending on the intended application, the adaptable silica chemistry enables the inclusion of a variety of functions. For targeting, imaging, and therapy, for example, many capabilities can be combined into a single particle [32–34]. In addition to evaluating their potential characteristics, silica NPs' interactions with cells have been better studied, particularly with regard to their toxicity, making them harmless for in vivo use [35]. SiO_2 NPs can make people more vulnerable to them through ingestion, cutaneous contact, and inhalation [36]. The aerodynamic and anatomic properties of nanoparticles can have an impact on how inhaled airborne silica particles behave in the respiratory system [37].

It has been demonstrated that exposure to human subjects might cause the cancerous condition silicosis [37, 38]. Furthermore, mice exposed to aerosols containing crystalline SiO_2 particles showed a significant increase in telomere length, which was associated with an increased risk of developing lung cancer [39]. Despite prior claims that amorphous SiO_2 NPs were less hazardous than their crystalline counterparts, investigative investigations have shown that the two NPs are quite equivalent [40]. After reviewing a large number of publications regarding amorphous SiO_2 NPs, Murugadoss et al. [41] were unable to determine if the exposure effects of amorphous silica nanoparticles (SiO_2 NPs) are comparable to those produced by crystalline micro SiO_2 NPs.

An earlier investigation demonstrated that Si/SiO2 quantum dots can trigger an inflammatory response in pulmonary fibroblasts [42]. Additionally, it was found that a brief, acute exposure to silica nanoparticles can cause elevated amounts of interleukins [43]. Adenocarcinoma human alveolar basal epithelial A549 cells' viability was reduced, while IL-1 and IL-6 levels were increased, according to Wu et al. [44]. Silica nanoparticles have been proven in numerous studies to be able to cause inflammation in human umbilical vein endothelial cells (HUVEC), mouse J774A.1 macrophage cells, and human hepatoma cells (Huh 7) when used in vitro [45, 46].

There have been a number of studies on the effects of nano-silica on human fibroblasts and how to improve the mechanical properties of concrete by incorporating nano-silica particles to cement. The literature is currently lacking in reviews pertaining to the use of silica nanoparticles to improve the mechanical properties of concrete. Additionally, no reviews have yet been undertaken of research that looked at how human fibroblasts react to silica nanoparticles. In light of this, this review examined the efficacy of silica nanoparticles in modifying the mechanical properties of cement concrete as well as how human fibroblasts react to them.

Properties of Nano-SiO_2

The enhanced pure amorphous silica powder known as nano-SiO_2 is a white powder [47]. Due to its exceptionally small particle size, it has a significant specific surface area, improved acceptable dispersion, strong surface adsorption, significant surface energy, and chemical purity [47]. Due to its unique properties, nano-silica performed an unrivaled role in physics, medicine, biology, chemistry, and other fields [48, 49]. Nano-SiO_2 can be divided into hydrophobic and hydrophilic types based on how hydrophilicity differs between them. Due to its successful dispersion in water, hydrophilic nano-SiO_2 is the type of nano-SiO_2 that is most frequently used in the creation of concrete. Most nano-SiO_2 used in concrete production has a particle size of under 100 nm [49].

By filling the pores between cement particles with significant amounts of fly ash at the nano-dimension, nano-SiO_2 can significantly improve the compressive strength of concretes containing a substantial volume of fly ash at an early stage and improve the pore size distribution [49]. Additionally, it has been demonstrated that when nano-SiO_2 particles are uniformly disseminated in the paste due to their increased activity, this results in the production of a huge number of nucleation sites that precipitate hydration derivatives that aid in the hydration of cement.

Mechanical Properties

Compressive Strength

Compressive strength can be explained as the capability of concrete to resist loads before failure [48]**.** Among the numerous investigations that have been carried out on the concrete, the examination of the compressive strength is the most significant, as it provides an assertion about its features [48]. The improvement of the compressive strength of concrete can be achieved by the addition of nano-SiO_2. An increase in nano-SiO_2 content toward the threshold content has been shown to increase the compressive strength of nano-SiO_2 modified concrete. Beyond the threshold value, a more elevated amount of nano-SiO_2 generally leads to a reduction in the compressive strength.

Isfahani et al. investigated the influence of adding varying nanosilica doses (0.5%, 1%, and 1.5% with respect to cement) on durability and compressive strength features of concrete with water/binder ratios 0.65, 0.55, and 0.5 [50]. Apparent chloride diffusion coefficient, water sorptivity, carbonation coefficient and electrical resistivity of concrete were examined. The outcome of the study revealed a significantly enhanced compressive strength for the case of water/binder = 0.65, while no change was observed for water/binder = 0.5. The water sorptivity was seen to reduce for water/binder = 0.55 as the nanosilica content increased. The introduction of 0.5% nanosilica lessen the evident diffusion coefficient of chloride for water/binder = 0.55 and 0.65; nevertheless, elevated dosages of nanosilica did not reduce as regards to the reference value. Figure 1 shows the environmental scanning electron microscope (ESEM) images of controlled concrete and concrete modified with addition of 1.5% nanosilica while Fig. 2 shows the effect of 0.5%, 1% and 1.5% nanosilica addition on concrete. Several studies have reported an optimum improvement of the compressive strength of concrete that was modified with 1.5% nano-SiO_2 content [51, 52]. The compressive strength of the concrete modified by the addition of nanosilica was reported to increase by 12%-17% at 28 days and 16%-25% at 7 days in comparison to conventional concrete. The key basis for the enhancement of the compressive strength of concrete is the pozzolanic reaction that took place between calcium hydroxide and nano-SiO_2, which facilitate the development of hydrated calcium silicate. Nonetheless, concrete free of nano-SiO_2 only depends on cement to hydrate to a little quantity of calcium silicate hydrate and the compressive strength of concrete is principally dependent on the quantity

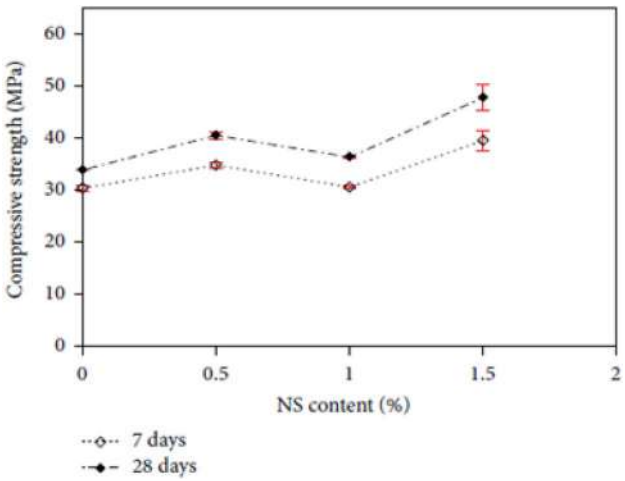

Fig. 2 Effect of nanosilica addition on concrete with different w/b; expressed as relative value of each parameter with respect to reference: **a** 0.5% NS addition, **b** 1% NS addition, and **c** 1.5% NS addition [50]

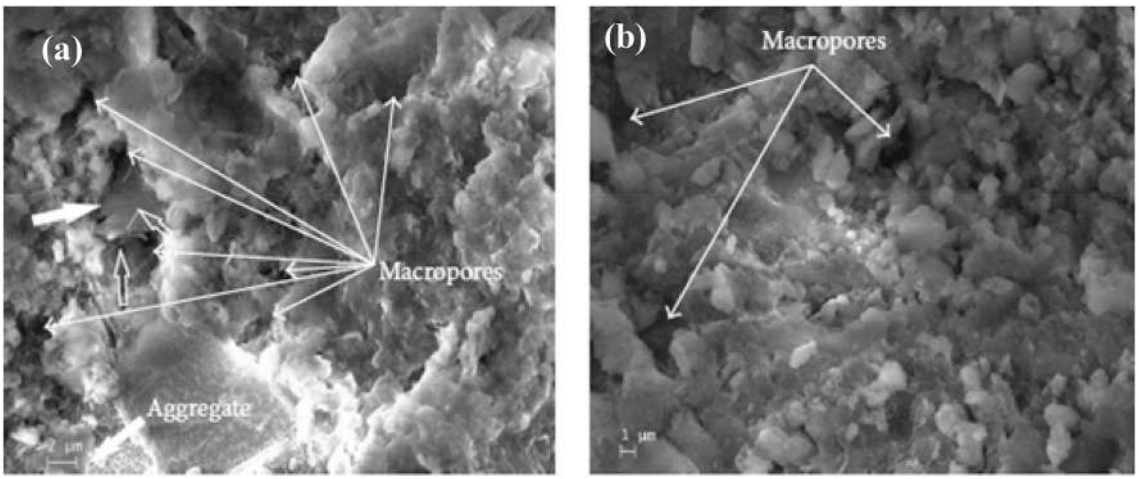

Fig. 1 ESEM images of concrete with w/b = 0.65: **a** control and **b** with 1.5% nanosilica addition [50]

of hydrated calcium silicate formed. As a consequence, the compressive strength of concrete free from nano-SiO_2 is usually low.

The impact of nano-silica on the compressive strength and workability of wood ash cement concrete was studied by Raheem et al. [53]. The results of their investigation indicated that the addition of nano-silica increased compressive strength. An ideal compressive strength of 27.53MP at 90 days was achieved with the addition of 1.5 percent nano-silica. The authors came to the conclusion that adding 1.5% nano-silica to wood ash concrete would best increase its workability and compressive strength. Due to the enhanced pozzolan characteristic of nano-SiO_2 particles, a prior study demonstrated that the timely strength enhancement influence of concrete modified with nano-silica is typically more visible [54, 55]. However, the number of nano-SiO_2 particles used in the pozzolanic reaction rapidly decreased with the interruption in curing time, which reduced the impact of nano-silica-modified concrete on later-stage compression enhancement.

Split Tensile Strength

An estimate of the maximum strain on a tension face of an unreinforced concrete beam at the point of collapse in bending is known as the split tensile strength [56]. To determine the load at which the concrete components may collapse, the tensile strength of concrete must be estimated [56]. By dividing the maximum applied load with appropriate geometrical variables, it is possible to investigate the split tensile strength [58]. Typically, hardened concrete is used to determine tensile strength. A slight change in the water to cement ratio, an increase in slump, the proportioning of the ingredients, etc., can have an impact on the anticipated concrete strength. The strength and stability of the buildings are consequently affected [58].

The split tensile strength of concrete can be improved by incorporating with silica nanoparticles. Alireza khaloo et al. investigated the splitting strength of diverse particle diameters of nano-SiO_2 by incorporating varying sizes of nano-SiO_2 into concrete [56]. They observed a more enhanced improvement in the splitting tensile strength of concrete modified with 12 nm nano-SiO_2 when compared to the concrete modified with 7 nm nano-SiO_2. In a completely different study, Reddy et al. investigated the split tensile strength of variable concrete modified with nano-silica-concrete cubes and 25% of Fly ash substitute for cement [57]. The split tensile strength of the entire types of the investigated concrete modified with nano-silica mixes was observed to be more superior to the traditional concrete. Interestingly, the split tensile strength of all the concrete mixes was observed to increase with time. Among the examined proportion of nano-silica blend, the concrete mix containing 1% nano-silica exhibited the highest strength when compared to other blended concrete mixes. Adetukasi et al. investigated the splitting tensile strength of fibre-reinforced concrete modified with polypropylene (PP) and nano-silica (NS) [58]. The outcome of their investigation recorded an optimum tensile strength of 3.48 N/mm^2 at 0.75% PP and 10% NS. The lowest tensile strength of 2.58 N/mm^2 was recorded by the standard concrete. Overall, the tensile strength of the concrete improved with an increase in the contents of both nanosilica and polypropylene fibre.

Fallah et al. substituted cement with 3% nano-SiO_2 to fabricate concrete and investigated the impacts of the modification on its splitting tensile strength [59]. The authors observed an improvement of 16.10% splitting tensile strength when compared to ordinary concrete. However, the modification of concrete with silica fume led to more improvement in the splitting tensile strength of the concrete when compared to the concrete modified with nano-SiO_2.

In comparison to the conventional concrete, an increment of 35% split tensile strength of nano-SiO_2 modified concrete was seen when the concrete was modified with 4% nano-SiO_2. The introduction of 0.3% steel fiber, 4% nano-SiO_2, 0.2% glass fiber and 0.2% polypropylene fiber boost the split tensile strength of nano-SiO_2 modified carbon fiber concrete by 57%, 90%, and 77%, respectively, in comparison to the standard concrete. This observation can be ascribed by the improvement of the interface strength between the aggregate and concrete matrix induced by the addition of nano-SiO_2 [59]. Palla et al. investigated the split tensile strength on concrete cylinders modified with nanosilica [41]. They observed an increase in the split tensile strength with increase in aging and the content of silica nanoparticles. About 9% compressive strength at 28 days in all the mixes was observed for the split tensile strength at 28 days of ageing. Figure 3 shows the Split tensile strength of the control concrete and concrete modified with silica nanoparticles. The reviewed studies shows that the addition of nano-SiO_2 to concrete does reinforce it, but likewise functions as a filling agent, which fills the concrete pores.

Flexural Strength

The ability of concrete to withstand bending forces applied perpendicular to its longitudinal axis is known as flexural strength. Beams, pavement, and slabs are just a few examples of the many structural components that can bend or flex. In order to withstand tensile or bending stresses, concrete compositions must have a flexural strength [60]. The trend of flexural strength and compressive strength in nano-silica-modified concrete is strikingly comparable. Due to differences in water-cement ratios, the ideal concentration of

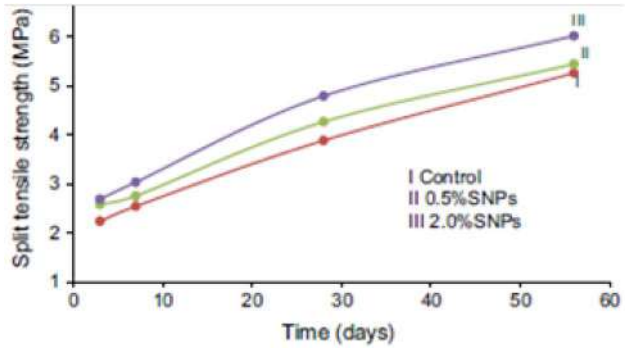

Fig. 3 Split tensile strength of control and SNPs incorporated specimens [40]

nano-SiO2 that effects the enhancement of flexural strength of concrete typically varies [61]. Ltifi et al. discovered an increase in the flexural strength of the mortar with an increase in the nano-SiO_2 content from 3 to 10% [62]. A similar investigation by Rong et al. observed the optimal flexural strength at curing for 3 days, 7 days, 28 days and 90 days for concrete modified with nano-SiO_2 content of 3% [51]. The significant performance of nano-SiO_2 on the flexural features of carbon fibre-reinforced concrete on treatment with high-temperature has been reported. Wu et al. discovered that nano-SiO_2 carbon fibre-reinforced concrete (NSCFRC) modified with 1wt% 0.15vol% carbon fibre and nano-SiO_2 exhibited the most heightened flexural strength at room temperature and improvement in residual flexural strength of NSCFRC with different content of nano-SiO_2 to a certain extent compared to carbon fibre concrete (0.15% carbon fibre) at varying temperatures [63]. Another study observed an optimal increment of 40% flexural strength of concrete-on-concrete modification of 4% carbon fibre content when compared to regular concrete [64]. The bending strength of fiber reinforced concrete increased by 53%, 67%, and 75%, respectively, on modification with nano-SiO_2 and different types of fibers (0.2% polypropylene fiber, 0.3% steel fiber and 0.2% glass fiber) in comparison to the regular concrete. This is mostly attributed to the improvement of the structural properties and adhesion between the interface region and fiber induced by the pozzolanic impact and nano-SiO_2 filler. Palla et al. examined the flexural strength of concrete prism modified with silica nanoparticles under four points bending at 28 days [60]. Figure 4 shows the SEM micrographs of the control and concrete modified with 2% silica nanoparticles at 28 days, while Fig. 5 shows the flexural strength of control and concrete modified with silica nanoparticles at 28 days. The outcome revealed a considerable enhancement in the flexural strength of the concrete modified with silica nanoparticles. The gained strength can be ascribed to secondary C–S–H gel development.

Challenges of Modifying Concrete with Nano-silica

Nano concrete exhibits outstanding performance due to its large surface area. At the same time, some difficulties in its usage have also received attention from intellectuals [64]. For instance, a heightened specific surface area has been shown to boost the performance of concrete, it also facilitates the aggregation of nano-SiO_2 which influences the dispersion effect in the water [64]. Also, the colloidal silica sol comprising monodisperse nanoparticles easily forms floccules and coatings on cement particle's surfaces

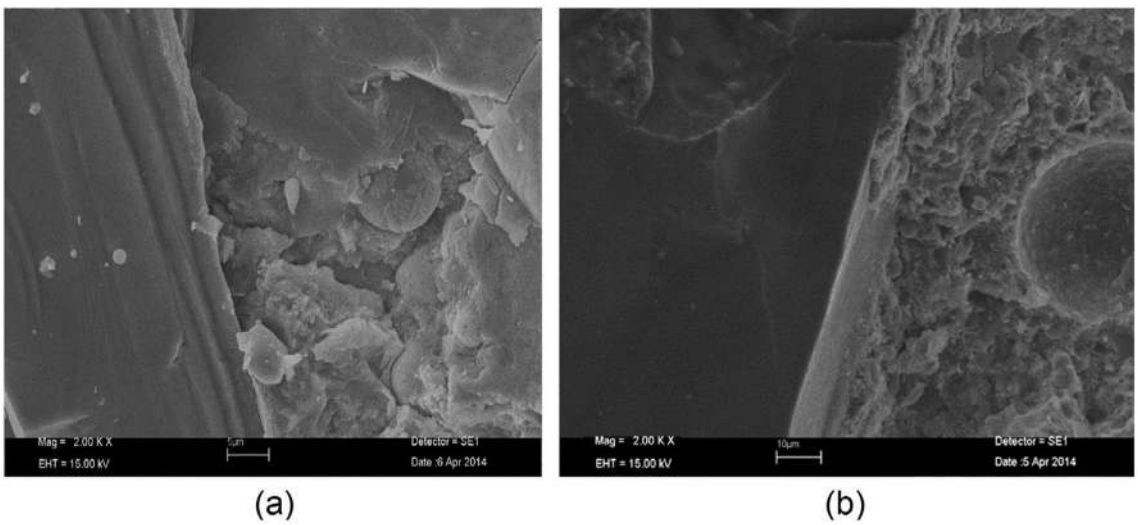

Fig. 4 SEM micrographs of control **a** and 2% SNPs incorporated **b** concrete specimens at 28 days of maturity [60]

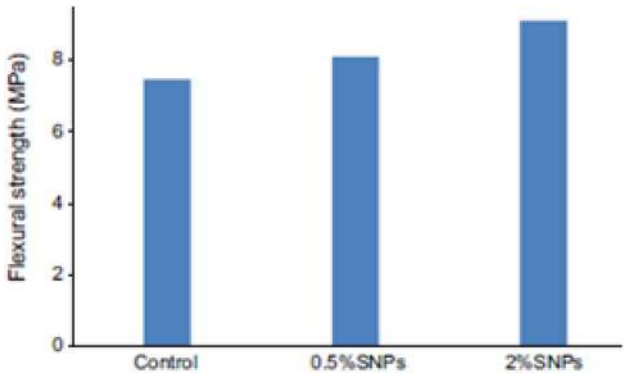

Fig. 5 Flexural strength of control and SNPs incorporated specimens at 28 days [60]

after combining with cement [65]. These floccules can freely retain unrestricted water, which is more apparent than the improvement induced by the hydration influence of nano-SiO_2. Thus, the usage of colloidal silica sol in concrete deserves consideration awareness.

Human Fibroblasts

A fibroblast is a type of biological cell that encourages the production of collagen and extracellular matrix, activates the stromal support system for animal tissues, and plays a crucial role in the healing of wounds [66]. The main cells that produce and maintain the extracellular matrix (ECM) in the connection of the tissue are fibroblasts [66]. Depending on their origin, fibroblasts play an important role in non-pathological tissue remodeling and diseases such fibrosis [67]. Fibrosis is a common pathogenic trait of chronic inflammatory diseases and can affect almost all bodily tissues [67]. Numerous biological functions and various cell types are impacted by fibrosis, particularly fibroblasts, which are activated when their phenotypic changes [68]. Fibroblasts are a complex and flexible collection of cells that originated from embryonic mesoderm and are engaged in several cellular processes in connective tissue [68]. As a result, they can be found in almost all bodily tissues and organs. In fibroblasts, an elliptical, speckled nucleus with two or more extra nucleoli is surrounded by branching cytoplasm [69]. The sizeable, tough endoplasmic reticulum that functional fibroblasts have can be used to identify them [69]. Fibroblasts that are not operating (also known as fibrocytes) are smaller, more spindle-shaped, and contain less rough or rugged endoplasmic reticulum [70]. Fibroblasts frequently localize in parallel clusters when congested, despite the fact that they are separated and deconstructed when the covering of a broad space is required [70]. Contrary to the epithelial cells that line body structures, fibroblasts do not form flat monolayers, nor are they hindered by a polarizing extension to a basal lamina on one side, though they may occasionally be helpful to basal lamina constituents (for example, subepithelial myofibroblasts in the intestine may secrete the α-2 chain-carrying integrant of the laminin, which is absent in regions of Contrary to epithelial cells, fibroblasts can move separately and gradually over a substrate [71].

In order to maintain the structural integrity of connective tissues, extracellular matrix precursors, which are continuously secreted by fibroblasts, are essential [72]. The antecedents of every element of the extracellular matrix, mostly a mixture of fibers and the ground substance, are secreted by fibroblasts [72]. The extracellular matrix compositions determine the physical characteristics of connective tissues. Similar to other connective tissue cells, fibroblasts can be produced from primitive mesenchyme [72]. As a result, they have the ability to carry the intermediate filament protein vimentin, which is used as a marker to identify their mesodermal root [73]. This investigation is not thorough, nevertheless, because epithelial cells cultivated in vitro on an adherent substrate may eventually express vimentin [73]. Epithelial-mesenchymal transition (EMT) is a process that, under certain circumstances, can cause epithelial cells to transform into fibroblasts [74]. On the other hand, in some circumstances fibroblasts may go through a mesenchymal to epithelial transition (MET) and become epithelia, assembling into a polarized, condensed, and lateral connected epithelial sheet [74]. This tactic is seen during many developmental processes, including cancer, wound healing, and the development of the notochord and nephron [74].

Response of Human Fibroblasts to Nanosilica

Growing use of goods based on nanoparticles and rising human exposure to NPs have sparked questions about how safe NPs are for people [75]. Inhalation is one of the main mechanistic routes through which people are exposed to NPs, and it is widely believed that when exposed to NPs, pulmonary inflammation is a regular phase [76] that initiates ongoing inflammation and results in irreparable lung injury [77]. One of the most well-known and often utilized NPs is silica, which has uses in paint, printer toner, paint additives, cosmetics, and medicine administration [77]. For instance, it has been demonstrated that exposure to Silica NPs causes a substantial rise in pro-inflammatory cytokines and immune cell infiltration in vivo in bronchoalveolar lavage fluids (BALFs) [41]. Additionally, this conclusion is supported by the clear logical connection between exposure to silica NPs and lung fibrosis in animal models [78]. Crystalline and amorphous silica have been classified by the International Agency for Research on Cancer (IARC) as group 1

and group 3 materials, respectively, based on the strength of the evidence supporting their carcinogenicity to people and experimental animals [79]. To better understand the underlying mechanisms, it is crucial to assess how human fibroblasts react when exposed to NPs, especially Silica NPs.

The probable harmful impacts in murine (3T3-L1) and human (WI-38) fibroblast cell lines of commercially available silica nanoparticles (NPs), Ludox CL (nominal size 21 nm) and CL-X (nominal size of 30 nm) were examined by Stępnik et al. with special attention to the impact over prolonged periods of exposure (72 h exposure up to 7 days) [80]. Both formulations differed in Physico-chemical features and displayed dissimilar stabilities in the cell culture medium that was utilized during the investigations. Aggregation of the CL-X silica NPs incorporated with ethylene glycol was observed at more elevated concentrations over the 72 h exposure. The NPs were observed to be more toxic to both mouse and human fibroblasts than the CL silica NPs coated with alumina, presumably in relation to the observed aggregation. Ludox CL silica NPs were seen to be exclusively toxic at elevated concentrations to the WI-38 cells (LDH and WST-1 assays) but not to the 3T3-L1 cells. However, the less stable ludox CL-X silica NPs over 72 h exposure were toxic to both cell lines in the assays. In the clonogenic assay, a concentration-reliant reduction in the surviving fraction of 3T3-L1 cells was instigated by both silica nanoparticles, with the Ludox CL-X silica NPs being more toxic. Examination of the cell cycle revealed an alteration in both cell lines at dissimilar phases with both investigated silica NPs. Ludox CL-X mixed with buthionine sulfoximine (γ-glutamylcysteine synthetase inhibitor) displayed an intense reduction in 3T3-L1 cell viability as opposed to the WI-38 cell line. The impact of nanomaterials, particularly, silica nanoparticles on cells can be achieved on prolong exposure.

Similar research was conducted by Voicu et al., who used a laser ablation technique to create stable SiO_2 nanoparticles and then looked at the inflammatory response in MRC-5 human lung fibroblasts up to 72 h after exposure to amorphous SiO_2 NPs [37]. To investigate the intracellular distribution of SiO2 NPs and cell survival, lactate dehydrogenase (LDH) testing and transmission electron microscopy (TEM) were used. Interleukin (IL)-1, IL-2, IL-6, IL-8, and IL-18 protein expression, lysosome formation, Nrf2, nitric oxide (NO) production, and TNF- production were also studied. The outcome of the experiment showed that exposure to the silica nanoparticles causes the level of lysosomes to increase with time (Fig. 6). While COX-2 and interleukins expressions were elevated, MMP-2 and MMP-9 expressions and activity decreased in a time-dependent manner. Negatively charged 10-nm SiO_2 NPs were incubated, which caused the overexpression of NF-kB and the downregulation of MMP activities, which promoted proinflammatory markers and anti-inflammatory IL-2. These effects are most likely the outcome of the physicochemical properties of the investigated NPs. It is simpler for silanol oxygen to attack the electrophilic carbonyl groups of protein peptide bonds and change their biological function and tridimensional conformation because silica nanoparticles have a nucleophilic nature. Numerous potential effects could arise at the level of the lung fibroblasts as a result of the oxidative stress and inflammation that are produced. The scientists came to the conclusion that 62.5 g/mL of SiO_2 NPs can cause an inflammatory response in MRC-5 cells. The results of this study can be used to enhance scar tissue, a fibrosis symptom, and the deposition of increasing amounts of extracellular matrix components.

It has been sufficiently documented that silica particles experience a process of dissolution in a biological medium, even if it is hindered by protein's existence [38]. Apart from earlier documentation on biopolymer-silica NPs that demonstrated the degradation prone nature of the bio-organic component over 48 h and visibility of silica fragments inside the cells [81], the possibility for intra-cellular dissolution of internalized particles started recording plausible success in 2012. If achieved, such an intracellular degradation operation may have numerous significant inferences: (i) outward liberation of soluble silicates in combination with particle exocytosis, and more significantly, if drug delivery usage is single out (ii) intra-cellular generation of silica oligomers or silicic acid that may affect universally their toxicity, (iii) stimulated the discharge of bioactive molecules originally entrapped within the silica colloids.

A previous study hypothesized that the uptake endosomal fate-exocytosis route must be examined for a prolonged duration (not less than 2 weeks) and that cautiousness must be used to differentiate soluble silica species from colloidal ones. Certainly, it has been authenticated that lengthier periods of exposure to silica particles could improve their uptake in HepG2 cells [82]. Also, they can instigate an increment in the local dose, exposure to the product of dissolution of the exocytosis or particles and cell-to-cell particles transfer [83]. Non-porous fluorescent silica nanoparticles with different surface charges and sizes (10 nm to 200 nm) were created by Quignard et al. [84], and their prolonged contact with human dermal fibroblasts was studied. The possible use of silica particles in cosmetics and their ability to penetrate skin served as the inspiration for this investigation. After 4 h of contact with human dermal fibroblasts at 37 °C, fluorescence microscopy analysis of the silica NPs indicated the presence of positively charged green 200 nm fluorescent nanoparticles nearby the fibroblast cells (Fig. 7a). These cells revealed the spindle-shaped morphology of typical fibroblasts, which was consistent with the nucleus membrane and the traditional red fluorescence signal of the WGA-AlexaFluor555-labeled external cell wall. Internalization of the NPs in intracellular

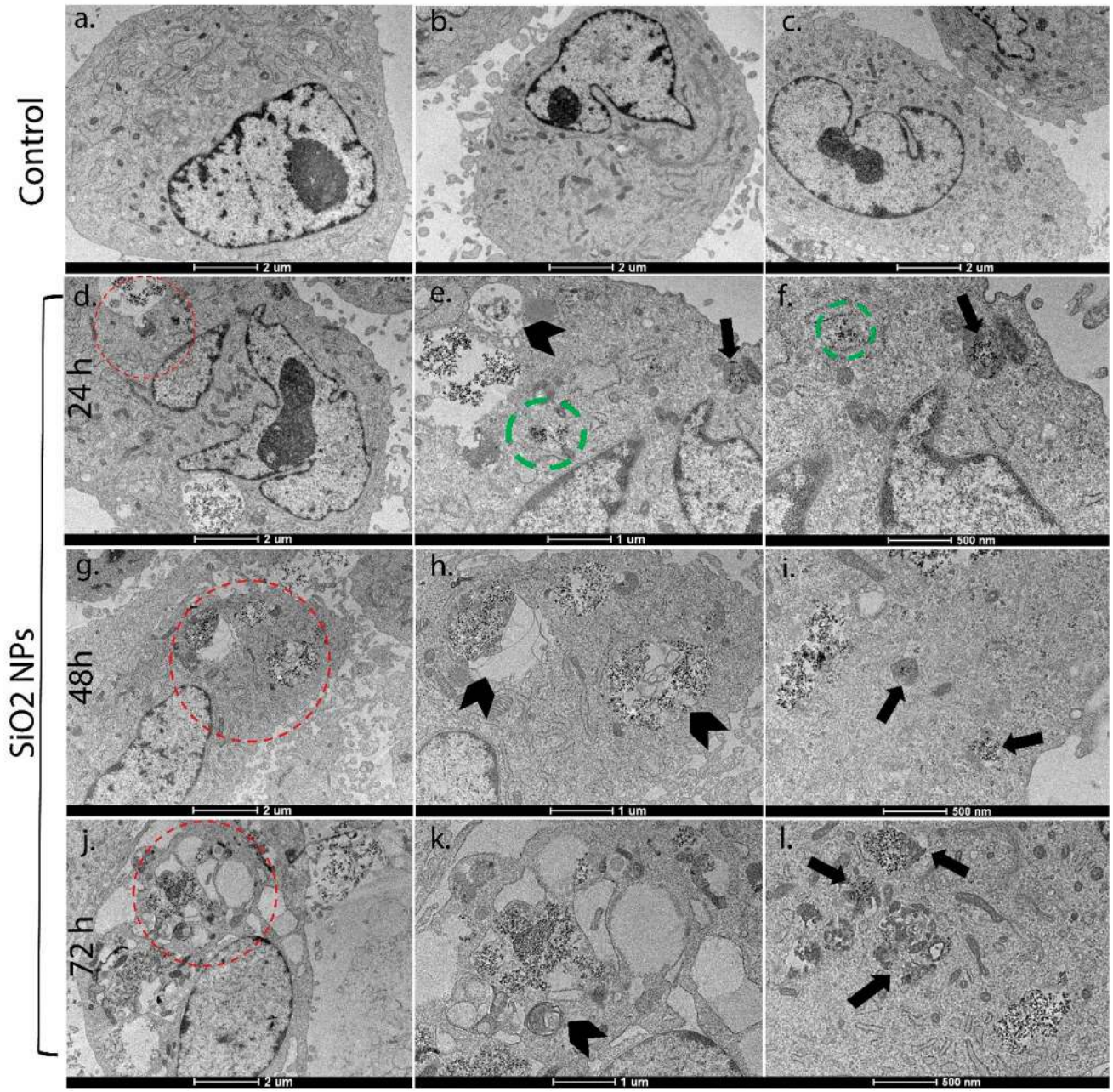

Fig. 6 Transmission electron microscopy images of MRC-5 cells with SiO_2 NPs treatment for 24 h **a**, 48 h **b**, and 72 h **c**. Silica nanoparticles (SiO_2 NPs) were not observed in untreated cell controls and the cellular structures were unchanged at 24 h, 48 h, and 72 h (**a**, **e**, **i**); Electron-dense SiO_2 NPs were spread in cytoplasm, lysosomes, and autophagic vacuoles in SiO_2 NP-treated cells, which increased with exposure time (**d**,**g**,**j**). The magnification view of the selected area (red circles) showed autophagic vacuoles (arrowheads) containing aggregated SiO_2 NPs (**e**, **h**, **k**); Figures (**f**, **i**, **l**) illustrated SiO_2 NPs-loaded lysosomes (arrows) and cytoplasmic SiO_2 NPs (green circle). Scale bars: 2 µm (**a**–**d**, **g**, **j**); 1 µm (**e**, **h**, **k**); 500 nm (**f**, **i**, **l**). Magnification: (**a**–**d**, **g**, **j**) 6000x; (**e**, **h**, **k**) 11,500x; (**f**, **i**, **l**) 20,500x. [37]

vesicles was seen after the positively charged 40 nm silica particles were exposed to the fibroblast cell. The cells appear longer when the positively charged 10 nm silica NPs are present, indicating some sort of physiological disruption. Very few silica particles are visible at the cell surface, and internal vesicles are more prevalent (Fig. 7c) The number of cells with unclear morphology that were detected for silica nanoparticles smaller than 10 nm was extremely low (Fig. 7d). These findings demonstrate that the negatively charged silica NPs considerably exacerbated the condition after 4 h. After 24 h of contact, the cells still retained their form and density while containing large numbers of

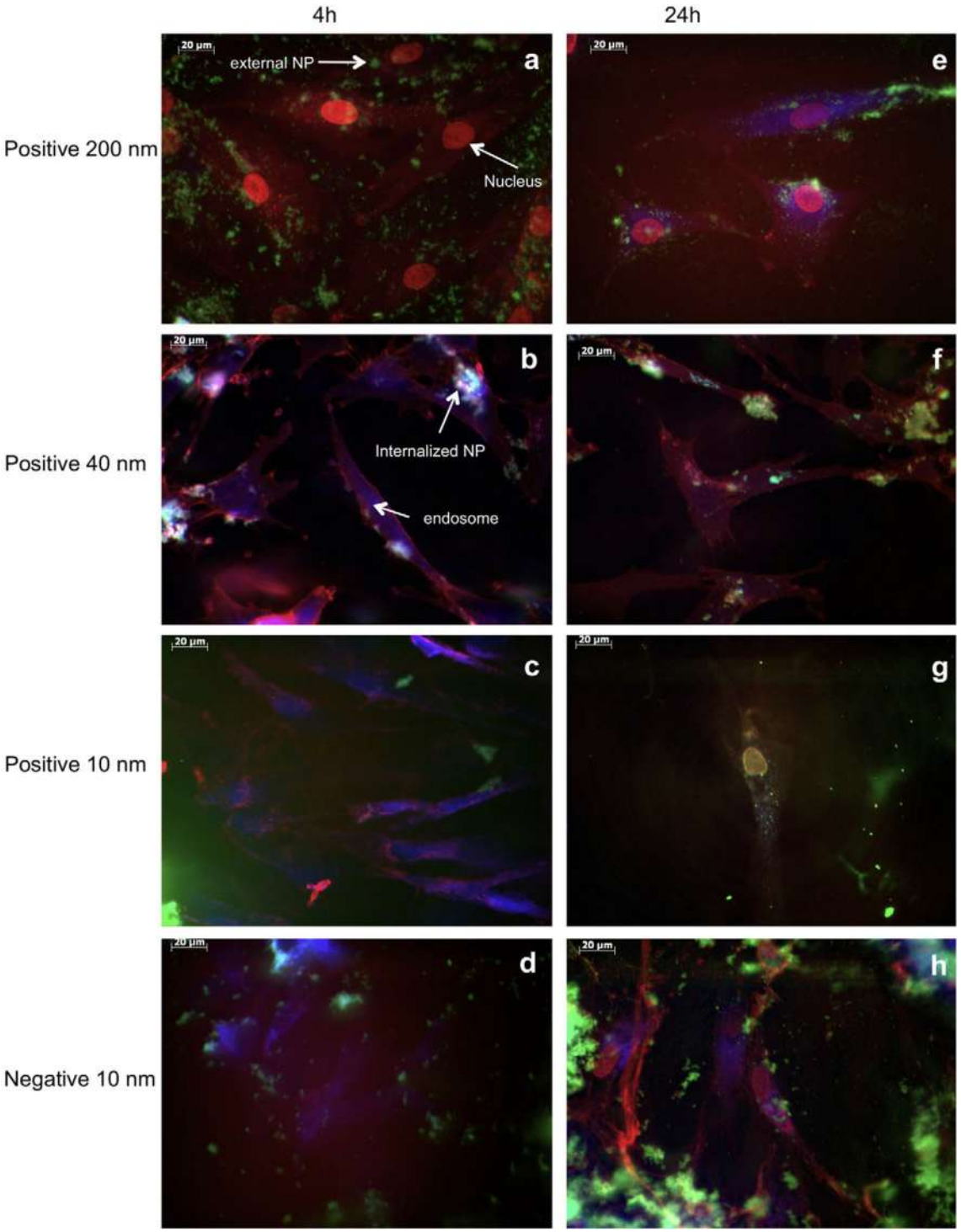

Fig. 7 Fluorescence optical imaging of human dermal fibroblast cells after 4 h (left-hand column) and 24 h (right-hand column) contact with (a,e) Si + 200, (b,f) Si + 40, (c,g) Si + 10 and (d, h) Si-10 nanoparticles. WGA-AlexaFluor555 and Lysosensor yellow-blue were used for red staining of the membrane and blue staining of the endosomes, respectively. Green fluorescence corresponds to FITC. (Scale bar: 20 mm) [84]

positively charged 200 nm and 40 nm silica nanoparticles as well as an increased density of intracellular vesicles (Fig. 7e, f). This might be a sign that they correlate with endosomes rather than lysosomes more closely. After 24 h of exposure, the positively charged 10 nm silica nanoparticles continued to elongate and fibroblast cell numbers decreased (Fig. 7g).

Negatively charged 10 nm silica nanoparticle aggregates with a significant reduction in cell density (Fig. 7h). It is possible to investigate the internalization process quantitatively by tracking the FITC signal's intracellular intensity. Within the first 24 h, positively and negatively charged 10 nm silica nanoparticles were significantly and quickly integrated in this study, however, the integration process of positively charged 200 nm and 40 nm silica nanoparticles was 10 times slower. The TEM study of the cells concurred with the aforementioned observations. This work demonstrates the potential use of non-porous silica particles in intracellular drug release mechanisms.

Collagen-based nanocomposites have been fabricated using silica NPs [85]. Desimone et al. synthesized collagen-silica NPs composite scaffolds for encapsulation of fibroblast cells, and demonstrated their biocompatibility [85]. The use of 3D matrices particularly bioglass nanoparticles for the repair of bones, [86], as well as for the elaboration of medicated wound dressings have been documented [87]. The fact that only spherical silica nanoparticles have so far been utilized explicate why described progress in mechanical features stayed modest [87]. Several studies have established reasonable interaction of collagen with the surface of nanosilica via attractive electrostatic interactions [88], but the effect of the interaction of particle morphology with collagen is limited in the literature. The interactions of silica nanoparticles in solution with mammalian cells has been comprehensively examined to illuminate the impact of both external (culture medium, type of cells, contact time, concentration) and intrinsic (morphology, including size, internal structure and surface chemistry) parameters [41, 89]. Existing facts about cell behavior on the surfaces of silica NPs points out the fundamental function of adhesion silica/ protein interactions that is greatly dependent on chemistry and surface topology [90]. Concentration and particle diameter have previously been shown to influence the proliferation in 2D /3D and fibroblast adhesion in 2D for collagen-silica nanocomposites [91]. This disparity was explained as a result of a myriads of factors comprising rugosity and modification of the surface chemistry, as well as change in the mechanical properties. In this regard, Shi et al. theorized that the usage of greatly anisotropic silica particles with one dimension equivalent to the scale of collagen fibrils and fibroblast cells would permit the promotion, and hence improved examination and interactions existing between the unalike constituents of the ternary protein-mineral-cell system [92]. The authors accomplished this goal by generating new collagen-based composite hydrogels within a broad concentration ranges and ratios using silica nanorods. The influence on human dermal fibroblast adhesion and proliferation as well as the rheological and structural features of the nanocomposites were investigated as a function of protein and nanoparticle content. Differentiation of the bio-mineral interactions regimes were correlated using mechanical responses, while the intrinsic properties of each component of the nanocomposite hydrogel was linked to the fate of seeded cells. High concentrations of collagen were advantageous to the mechanical features of the nanocomposite materials whereas the existence of silica nanorods in the nanocomposiites at high or low content could lead to an outcome that is very encouraging. Electron microscopy analysis shows good homogeneity of NPs with rodlike shape and powerful biomineral interactions, highlighting the factual composite nature of these materials (Figs. 7, 8, 9). In contrast, the investigations of proliferation and adhesion showed that, in spite of these interactions, fibroblasts can distinguish between the inorganic phases and the protein and also infiltrate the collagen network to restrict uninterrupted contact with silica. The authors concluded that such a divergence between biological responses and physico-chemical properties has key implications for the estimation of the in vivo fate of nanocomposite biomaterials.

The effects of surface nano-patterning on oral early Streptococcus mitis adhesion, the opportunistic pathogen Staphylococcus aureus adhesion, commensal colonizer adhesion, and human fibroblasts adhesion in a laminar flow cell were investigated by Kallas et al. [93]. In order to create nanostructured surfaces, glass substrates were functionalized with 40 nm SiO_2 nanoparticles. By creating gradients in nanoparticle surface coverage, the impact of nanoparticle spacing within a single experiment was examined. An examination of bacterial adhesion after five minutes of contact involved exposing surfaces to a flow using a laminar flow chamber. To further examine the effect of the particles on human cells, the growth of primary human dermal fibroblasts (HDFa) and the emergence of focal adhesion were evaluated at 4 and 24 h. In comparison to smooth surfaces, S. mitis and S. aureus adhesion was decreased on surfaces functionalized with nanoparticles, increasing the surface coverage of the particles. According to the regression analysis, S. mitis was more sensitive to surface modification than S. aureus. For the investigation of human dermal fibroblasts, the authors found that cells cultivated on the assembled component of the bi-functional nanostructured surfaces for both 4 and 24 h had less focal adhesions. We explain these results by the few sites of contact between the cells and the nanoparticle-provided substrate. The findings of this study could be applied to future prostheses and implant surfaces to reduce bacterial adherence.

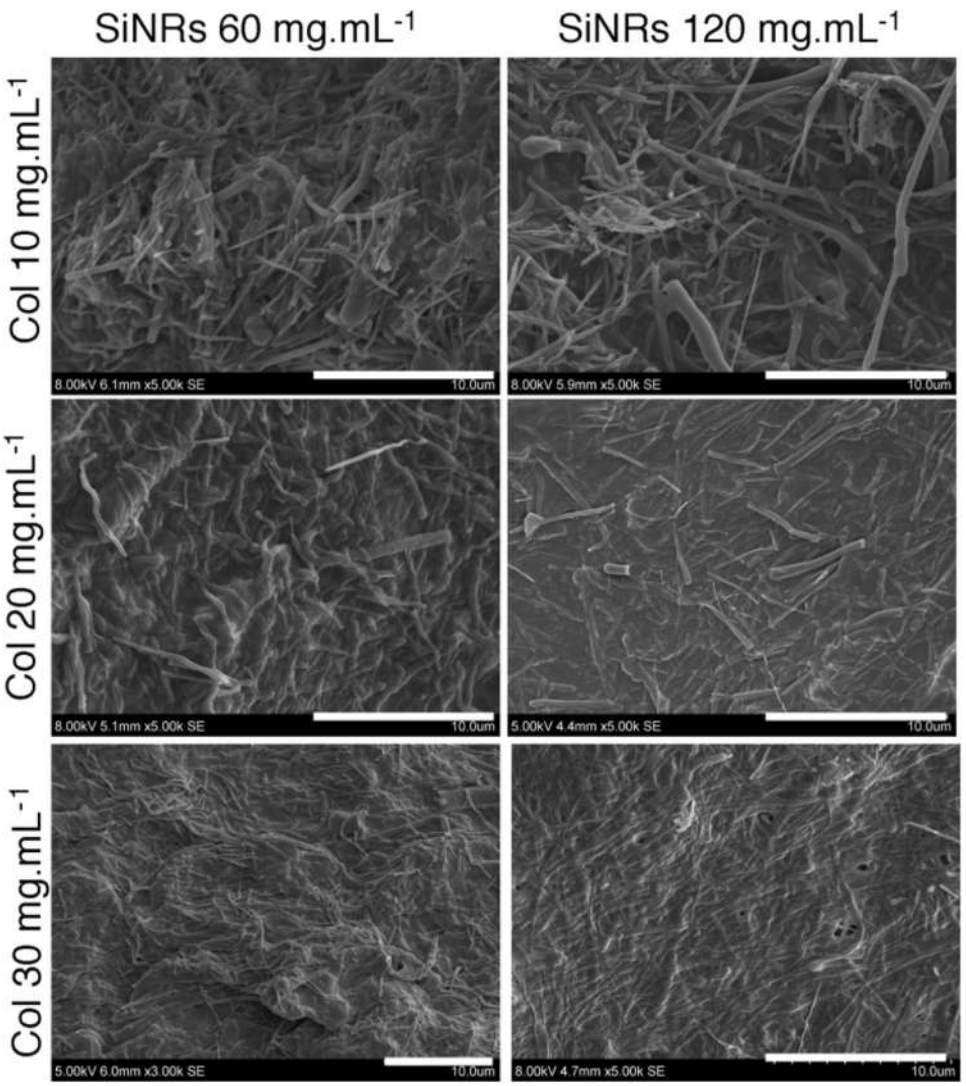

Fig. 8 Selected SEM images of SiNRs–collagen nanocomposites at collagen concentrations 10, 20, and 30 mg mL^{-1} and silica concentration of 60 and 120 mg $mL.^{-1}$ (scale bar = 10 µm). SEM, scanning electron microscopy; SiNRs, silica nanorods [92]

Conclusion

We briefly reviewed how the mechanical properties of concrete such as compressive strength, split tensile strength, and flexural strength are affected by the addition of nano-SiO_2. The incorporation of nano-SiO_2 considerably enhances the aforementioned qualities, according to a review of numerous studies. One significant drawback of using nano-SiO2 sol is that, after mixing with cement, it quickly produces floccules and coatings on the surfaces of the cement particles, making it freely retain unlimited water, which is more noticeable than the benefit brought on by the influence of nano-SiO_2. To address this issue, additional research must be conducted. The impact of silica nanoparticles on human fibroblast response was also examined in this study. It has been demonstrated that the interaction of silica nanoparticles with human fibroblast cells results in an inflammatory response, internalization of the NPs in intracellular vesicles, improvement in their uptake in HepG2 cells with increased periods of silica NPs exposure, a decrease in the number of focal adhesions for cells cultured on the assembled portion of the bi-functional silica nanostructured surfaces, significant cell deterioration, elongation and reduction, etc. The controlled interaction of silica nanoparticles with human fibroblast cells may be utilized for a number of practical applications, such as cosmetics, intracellular drug release systems, the deposition of increasing amounts of extracellular matrix components, the progression of scar tissue, a defining feature of fibrosis, the estimation of the in vivo fate of biomaterials, and the design of potential prostheses and implant surfaces to lessen bacterial adhesion.

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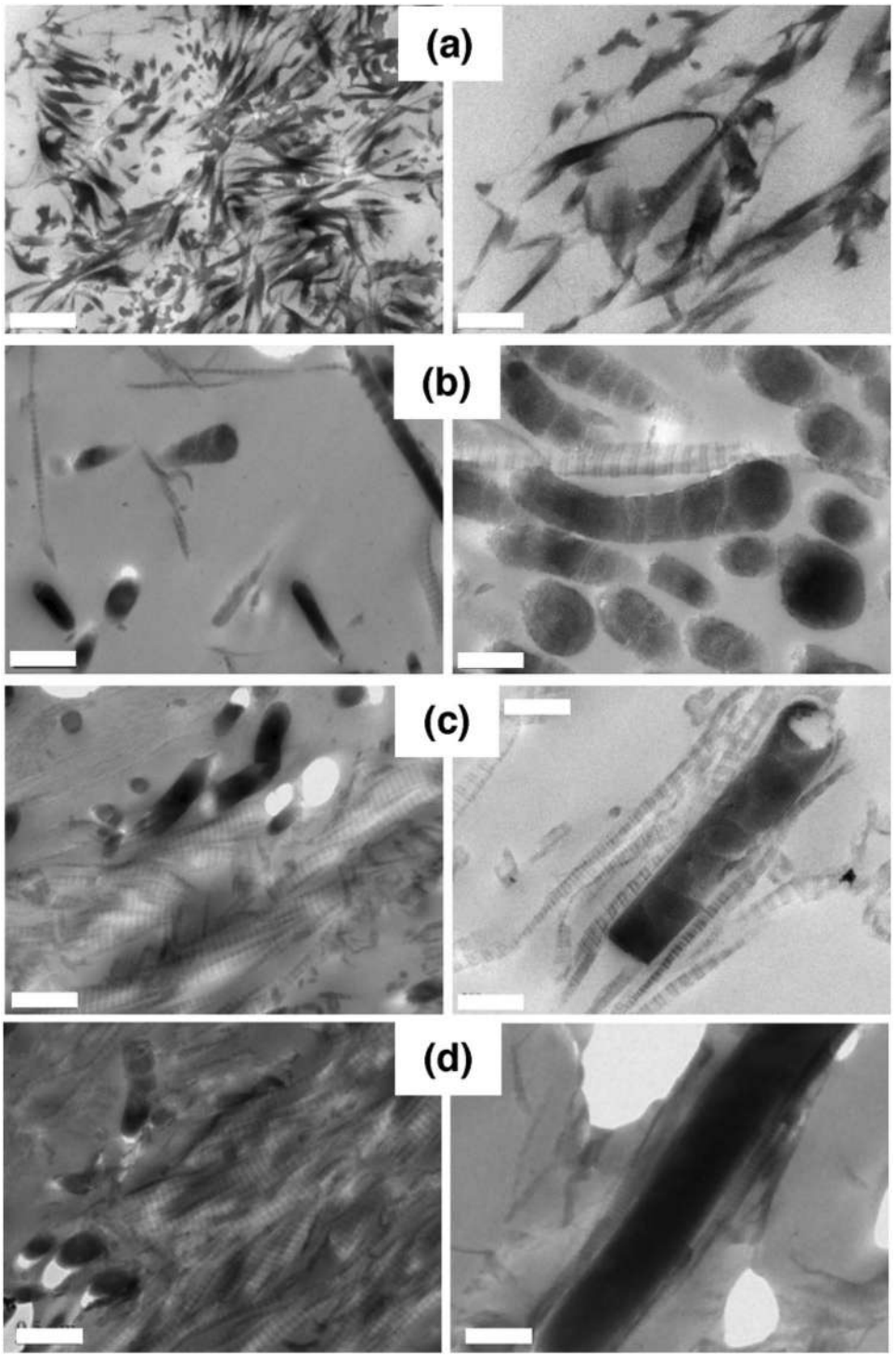

Fig. 9 TEM of **a** 20 mg mL^{-1} collagen. **b** 10 mg mL^{-1} collagen, 120 mg mL^{-1} SiNRs. **c** 20 mg mL^{-1} collagen, 60 mg mL^{-1} SiNRs. **d** 30 mg mL^{-1} collagen, 30 mg $mL.^{-1}$ SiNRs. Scale bar: left-hand column: 500 nm; right-hand column: 200 nm. SiNRs, silica nanorods; TEM, transmission electron microscopy [92]

Declarations

Conflict of interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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